DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1962

HEARINGS

BEFORE THE

SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS HOUSE OF REPRESENTATIVES

EIGHTY-SEVENTH CONGRESS

FIRST SESSION

SUBCOMMITTEE ON DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE AND RELATED AGENCIES APPROPRIATIONS

JOHN E. FOGARTY, Rhode Island, ***Chairman***

WINFIELD K. DENTON, Indiana	MELVIN R. LAIRD, Wisconsin
FRED MARSHALL, Minnesota	ROBERT H. MICHEL, Illinois

ROBERT M. MOYER, *Staff Assistant to Subcommittee*

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PART 2

Public Health Service

Printed for the use of the Committee on Appropriations

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U.S. Congress. House. Committee on Appropriations

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DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1962

Thursday, March 16, 1961.

PUBLIC HEALTH SERVICE

WITNESSES

DR. LUTHER L. TERRY, SURGEON GENERAL
DR. JOHN D. PORTERFIELD, DEPUTY SURGEON GENERAL
DR. JAMES V. LOWRY, CHIEF, BUREAU OF MEDICAL SERVICES
DR. THEODORE J. BAUER, CHIEF, BUREAU OF STATE SERVICES
DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT J. ANDERSON, DEPUTY CHIEF, BUREAU OF STATE SERVICES
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Mr. Fogarty. The committee will come to order.

We have before us this afternoon our new Surgeon General, whom I have known for some time. Dr. Terry, we are very pleased to have you with us today, and I am sure that those of us who know you think that you are going to do a good job. You have a very sympathetic committee with which to deal here.

Now, with any new appointee, we ask them to give us some of their background for the record. So before you start, I think that would be in order.

BIOGRAPHY OF SURGEON GENERAL

Dr. Terry. Thank you, Mr. Chairman.

I was born and reared in Red Level, Ala., a small town in south Alabama where my father practiced medicine for 33 years. Graduating from the local high school, I attended Birmingham Southern College, receiving my B.S. degree in 1931, then Tulane University Medical School, where I received my doctor of medicine degree in 1935.

Subsequent thereto, I had hospital training in Birmingham, Ala., and 3 years in Cleveland, Ohio, in the university hospitals and in Cleveland City Hospital.

Thereafter, I went to Washington University in St. Louis, where I spent a year working as an instructor in the department of medicine and as a research fellow. Thereafter, I was offered a position; in fact, a full-time position on the medical faculty branch of the University of Texas at Galveston, Tex. I went there as an instructor, remained for 3 years from early 1940 to late 1942. During that time, I served in both the department of medicine and the department of preventive medicine and public health, and was made an associate professor shortly before I left there to enter the Public Health Service in 1942.

In September 1942, I entered the Public Health Service and was assigned to active duty at the Baltimore Hospital. I remained at the Baltimore Public Health Service Hospital from 1942 to 1953. Actually, during the last 3 years of that——

Mr. FOGARTY. I think at that point you were carrying on a very important program in Baltimore.

Dr. TERRY. Yes; we were, sir.

Mr. FOGARTY. Why do you not just tell us a little bit about that too.

Dr. TERRY. All right, sir.

When I first came to the hospital in 1942, it was during the early stages of the war; most of our attention was concentrated on rendering medical care of the finest quality and as rapidly as we could.

Along at that time, however, one of the things that became immediately evident to me, just entering the service, was that our hospitals at that time did not have formal training programs beyond the internship level. So that I began to collaborate with some of my friends and associates at Johns Hopkins University, and I was given an appointment on the Hopkins staff, which I have kept up until recently, which was a part-time, no-pay appointment.

But in working with them, we developed, if not the first, one of the first medical residency training programs in the Public Health Service hospitals. Our program was first recognized by the Council on Medical Education in 1944.

Subsequent to that, we developed residency training programs in essentially all of the specialties in that hospital.

During that time, I was doing some research, clinical research, as we had the time and ability to do it. I was doing some teaching at Hopkins, usually a half day once a week, and continuing with the medical care program and the training of my resident staff there.

By 1950, shortly after the National Heart Institute was created, I was approached by the National Heart Institute and asked if I would accept a position as chief of one of the laboratories in the Heart Institute. As a matter of fact, Dr. Shannon here approached me at that time.

At that time I was given an appointment as chief of the Laboratory of General Medicine and Experimental Therapeutics of the Heart Institute, with several objectives in mind. One was that we would begin, while I was still there in Baltimore and before clinical facilities were available at Bethesda in the Clinical Center, to assemble a team, a clinical research team, which could subsequently be moved to the Clinical Center.

I continued as Chief of the Medical Service there at the hospital. I was also very active in shuffling back and forth between Baltimore and Bethesda to make the plans and obtain equipment and get things set for the operation of the research program, particularly the clinical research program at Bethesda. I acted in this dual capacity from 1950 to 1953.

In the spring of 1953, shortly before the clinical center was opened, I moved over to Bethesda. In early July 1953, we brought our entire team, consisting of doctors and technicians and animal caretakers and other assistants, experimental animals, and even eight patients with us that we had in the Baltimore Hospital. And these were the first eight patients that were admitted to the clinical center.

Since then, I have continued in the program of the National Heart Institute, and have, during that time, served as the person in charge of our clinical program, in charge of our Laboratory of General Medicine and Experimental Therapeutics.

This was the largest laboratory that we had in the Heart Institute and was broken up into three distinct segments. I had administrative responsibility for all three sections of this laboratory. One of the sections was a section on clinical endocrinology, under Dr. Fred Barter, who is one of our very distinguished investigators. He was quite capable of operating the section, and I really did not participate in the routine details of the day-to-day operation there.

The second section was our section of cardiodynamics, which was under the direction of Dr. Robert Grant, who is also a well-respected, established investigator and physician. He, too, largely ran his section insofar as day-to-day operations were concerned.

The third section of our laboratory was the section of experimental therapeutics. This was the section in which I had my outlet in terms of the research activities in which I was involved and the day-to-day operation of a research team.

During this period of time, we were studying many problems in our section on experimental therapeutics. One of the principal problems that we were working on for some period of time, and still are, for that matter, is the matter of hypertension. We have had a great interest in hypertension. We, early, got onto some of the enzyme inhibiting agents which were thought possibly to have some effect in hypertension, also in angina, and began working with those.

We did some work in the early stages with Marsalid. Another compound was JB 516, or Catron. This was a very promising and a very interesting drug. After we had been working with it for a year and using it in many patients, we then discovered that the drug had side effects; namely, toxicity on the eye or on vision. Some patients who took larger doses of the drug, developed color blindness and also developed areas of scotomata—points of blindness in the retina.

It was an interesting thing that we had been going along for a year and were quite enthusiastic about this drug, and one morning one of our patients walked in and he said, "Doctor, I almost got killed down at this intersection." Then we began to ask him what happened. Well, it happened that he had gone right through the middle of a red light. Since he had developed color blindness without being aware that he had developed it, he did not know that he was running through a red light, and almost had a serious collision.

It turned out that this drug, in the doses which were necessary to really get the effects that we needed in the patients of moderate or more severe hypertension, tended, in a fairly large percentage of the cases, to have these side effects. This obviously restricted its use, and it is hardly used at all in hypertension today.

More recently, we have been working with other drugs, most of which are not on the market yet, have been designated by experimental numbers, which are drugs that interfere with the enzyme systems in the production of the amines, such as adrenaline and noradrenaline and serotonin. We have had a very active clinical and laboratory investigative program going on this subject.

In August 1958, I was invited to accept the position as Assistant Director of the Heart Institute under Dr. Watt. This I did, and was able to continue with some of my clinical studies as well as serving in this administrative position.

Actually, during the last year that I was in this position, my time for clinical duties got seriously curtailed when Dr. Watt, as the Director, was assigned as Special Assistant to the Secretary for the White House Conference on Aging and he spent approximately half of his time downtown on this program. During his absence, I was the Acting Director of the Heart Institute.

The amount of time that he had to spend downtown, in addition to the official trips that he had to make amounted to the fact that I was Acting Director of the Heart Institute during a considerable portion of that last year.

However, I was able to continue with some of my clinical responsibilities. I did give up the job as Chief of the Section of Experimental Therapeutics. Dr. Albert Sjoerdsma, who was a physician who had developed there with us, took over this responsibility; and during the last 2½ years that I served there, I worked as a clinical investigator associated with this team; I was one of the staff members of the team, but was not in charge of this particular group.

This brings me down, Mr. Chairman, to current time.

Mr. Fogarty. Well, that is quite a background.

Dr. Terry. I hope I did not go into too much detail, sir.

Mr. Fogarty. No, I think it is a good start.

Now do you want to read your statement?

Dr. Terry. If I may, sir.

Mr. Fogarty. All right, go right ahead.

General Statement of the Surgeon General

Dr. Terry. Mr. Chairman and members of the committee, it is a great pleasure to make my first appearance before this committee as Surgeon General of the Public Health Service. You gentlemen are well aware, as I am, that the responsibilities of my new position have increased enormously in the past 15 years.

Twenty-three new programs requiring the attention of this distinguished committee have been established in the Public Health Service since 1945. Appropriations to the Service increased from $128 million for the fiscal year 1945 to $1,038 million for 1961. Of the total $6.4 billion appropriated in that period, $1,146 million were for the construction of facilities for our expanding Public Health Service programs. Included in this new construction are the Clinical Center and other research facilities at the National Institutes of Health, the Sanitary Engineering Center at Cincinnati, hospitals and other health facilities for American Indians and Alaska natives, and the National Library of Medicine at Bethesda, Md., which will be opened in November 1961. The Communicable Disease Center at Atlanta was constructed at a cost of about $12 million under lease purchase arrangements through the General Services Administration.

The major increases in annual expenditures of the Public Health Service have been to augment Federal assistance to the Nation's total effort for improved health. This has involved grants and other forms of support for medical research; training of certain categories of personnel; construction of hospitals and other needed facilities; establishment of programs to combat environmental hazards; expansion of disease control and other community health services. This fiscal year, 1961, more than 70 percent of the funds appropriated to the Public Health Service will be expended by State governments, local communities, public, and private nonprofit institutions for these purposes.

1962 BUDGET

The Public Health Service budget for 1962, as amended by President Kennedy, totals a little over $1.1 billion. The budget includes $59,046,000 for the Indian health program, which is being considered by the Subcommittee on Department of the Interior. The total budget is designed to support all direct activities of the Public Health Service, as well as all of our grant programs for research, training, construction of non-Federal facilities, community health and environmental health services. The funds requested for 1962 amount to about $75 million more than was or will be programed for 1961.

Mr. Chairman, I have not been in my new job long enough to familiarize myself thoroughly with the structure of the budget now before you. With your permission, I shall leave the technical details to our program operators and budget officers.

I must say, also, that I shall need further time to determine to my own satisfaction just where lie the greatest needs for strengthening the PHS' long-range contributions to national health.

BUDGET AMENDMENTS

However, the revisions of the 1962 budget, which we have developed within the past 6 weeks, are designed to speed up activities in several areas destined for major expansion in the near future.

For example, we are requesting an additional $35 million for construction grants under the Hill-Burton program. This would bring the 1962 appropriation for aid to hospital and medical facilities construction to the same level as this year's; namely, $188 million.

Also, an addition to the initial National Institutes of Health request would permit continued expansion in the Nation's medical research and research training effort. The revised estimate of $583 million is $43 million above the initial 1962 request and $23 million above the 1961 appropriation. The major portion of this increase (about $31 million) would be used for the support of new research through the regular grant program of the National Institutes of Health. When reserves, transfers, and nonrecurring expenses are taken into consideration, the NIH 1962 budget as amended provides an increase of $73.1 million over 1961.

Another important revision is the addition of $2 million to the original request of $61,750,000 for community health activities. Specifically, these funds would be expended for the development of cooperative projects in local communities, designed to improve services for care of the chronically ill and the aged.

Although a modest increase for these purposes was included in the original request, I am convinced that we can and must move more rapidly than was anticipated in this area. Services in nursing homes throughout the country urgently need improvement. Community services, such as home care and homemaker programs, need to be started in hundreds of localities which have not been able to obtain the skilled personnel to organize and sustain these activities in the initial period. The revised estimate would make it possible for the Public Health Service to help more communities to get a start in the next fiscal year.

If legislation now before the Congress is enacted, we shall need much larger appropriations for community health services, nursing home construction grants, and hospital research grants. All of these have the same broad aim: to strengthen and improve community services for care of the sick and for the prevention of disease and prolonged disability.

I do not wish to imply that no progress was anticipated in the original Public Health Service budget for 1962. An increase of about $7 million over the 1961 estimate is requested for environmental health. Also, the full authorized sum of $50 million is requested for grants to municipalities for the construction of waste treatment facilities. I heartily endorse these increased estimates and expect rapid development of our environmental research, training, and control activities in the immediate future.

MARINE HOSPITALS

Thanks to the interest and action of this committee, appropriations to our Public Health Service hospitals have been increased to a level that will permit us to provide a quality of medical care closer to the requirements of present-day medicine. The very valuable clinical resources of our hospitals also are being utilized to a greater extent in medical research. Our physicians and dentists have better opportunities to conduct useful investigations in cooperation with nearby medical centers. I am not prepared to say that we have reached the zenith in the staffing patterns of all of our hospitals.

Moreover, there are critical problems related to the quality of our facilities. We have made progress, however; and since I spent my first 10 years in the Public Health Service as a clinician and clinical investigator at our Baltimore Hospital, I am especially grateful to this committee for its support in this area.

REORGANIZATION OF PHS

Mr. Chairman, I am glad to report that considerable progress has been made in the reorganization of the Public Health Service along the lines recommended to the former Surgeon General, Dr. Leroy E. Burney, by a Service study group in 1960, and by him to the Secretary of Health, Education, and Welfare and the 86th Congress.

I am aware of the great interest expressed by this committee and other congressional groups in a more effective grouping of our environmental health activities. As you know, Mr. Chairman, this led to the broader proposals which would equip the Public Health Service to manage its expanding programs more efficiently.

Although much could be accomplished—and has been accomplished—by administrative action within our present statutory framework of the four "named" bureaus, it will require legislation to implement the proposals for two new bureaus in place of our current Bureau of State Services. Bills were introduced in the 86th Congress too late for action. Similar legislation will be introduced in the 87th Congress, and we anticipate its enactment.

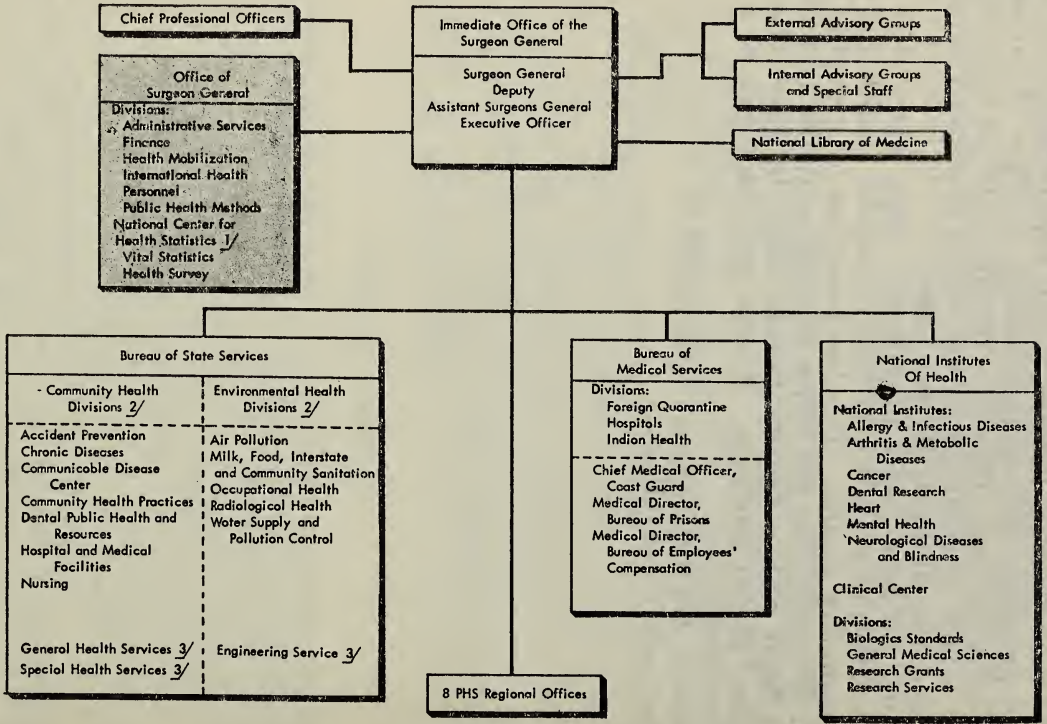
Meanwhile, we have taken preparatory steps which will allow prompt activation of a Bureau of Environmental Health and a Bureau of Community Health. This has been done by grouping in the Bureau of State Services the major existing activities in those two distinctive fields with a Deputy Bureau Chief in direct charge of environmental health programs. I have with me copies of a chart showing these groups——

Mr. FOGARTY. We shall put that in the record.

(The chart referred to follows:)

CHART 3

PUBLIC HEALTH SERVICE - 1960


Chief Professional Officers
Immediate Office of the Surgeon General
Surgeon General
Deputy
Assistant Surgeons General
Executive Officer
External Advisory Groups
Internal Advisory Groups and Special Staff
National Library of Medicine
Office of Surgeon General
Divisions:
Administrative Services
Finance
Health Mobilization
International Health
Personnel
Public Health Methods
National Center for Health Statistics 1/
Vital Statistics
Health Survey
Bureau of State Services
Community Health Divisions 2/
Accident Prevention
Chronic Diseases
Communicable Disease Center
Community Health Practices
Dental Public Health and Resources
Hospital and Medical Facilities
Nursing
General Health Services 3/
Special Health Services 3/
Environmental Health Divisions 2/
Air Pollution
Milk, Food, Interstate and Community Sanitation
Occupational Health
Radiological Health
Water Supply and Pollution Control
Engineering Service 3/
8 PHS Regional Offices
Bureau of Medical Services
Divisions:
Foreign Quarantine
Hospitals
Indian Health
Chief Medical Officer, Coast Guard
Medical Director, Bureau of Prisons
Medical Director, Bureau of Employees' Compensation
National Institutes Of Health
National Institutes:
Allergy & Infectious Diseases
Arthritis & Metabolic Diseases
Cancer
Dental Research
Heart
Mental Health
Neurological Diseases and Blindness
Clinical Center
Divisions:
Biologics Standards
General Medical Sciences
Research Grants
Research Services

1/ Separate organizational status similar to the National Library of Medicine is proposed under the reorganization plan.

2/ These groupings would become bureaus under the reorganization plan. Some divisions not listed but recommended by reorganization plan are still under consideration.

3/ To be abolished as reorganization progresses.

December, 1960

Dr. TERRY. The chart shows these groupings, as well as the operating divisions created or transferred for these purposes. It is obvious, I believe, that the retention of these numerous, varied, and growing programs in one bureau would prove most unsatisfactory to the Congress, the executive branch, and to the public groups served by the programs.

The chart shows also that we have established a National Center for Health Statistics, combining the National Office of Vital Statistics and the National Health Survey under one Director. The Center has separate, but not bureau-level status, as does the National Library of Medicine.

As a result of these preliminary changes, I am not the only new appointee who will appear before this committee in support of the PHS 1962 budget. I shall depend on Dr. Porterfield, Dr. Bauer, Dr. Lowry, and Dr. Shannon to introduce the new program operators as they come before the committee.

In conclusion, I should like to say, Mr. Chairman, that I look forward with the keenest anticipation to the development of our Public Health Service programs under the administration of President Kennedy and Secretary Ribicoff. I know that the Public Health Service shares my enthusiasm. The President's proposals for health and for natural resources include a beginning or an extension of national action toward every major goal proposed by the Public Health Service and other responsible health organizations in our country for the past 25 years.

We welcome the hard work that may fall to our lot in implementing those proposals. We know that our efforts in cooperation with the Nation's public and private health forces can have but one result: more and better health services for the American people.

Mr. Chairman and members of the committee, I shall be happy to answer any questions which you should like to submit to me.

Mr. FOGARTY. Thank you, Doctor.

ADEQUACY OF THE 1962 BUDGET

You and the Secretary seem to be quite enthusiastic about the budget and think we are moving ahead at a much faster rate than I do. I disagreed with the Secretary on the progress that this budget will allow when he was here Monday. We had some confusion Monday, because on the one hand we had Mr. Cohen and his task force report saying in effect we ought to stand still as far as medical research is concerned; and then we had your very able special assistant to the Secretary, Mr. Jones, defending a budget that he said ought to have been appropriated last year for about $130 million more than you are asking this year. Then the Secretary is in between.

I made the suggestion that we ought to be spending about $100 million more on the National Institutes of Health than you are asking for. If the committee decided to increase this appropriation by $100 million, do you think you could use it?

Dr. TERRY. $100 million above the figure that we have recommended?

Mr. FOGARTY. Yes.

Dr. TERRY. That is a very difficult question to answer, Mr. Chairman.

Mr. Fogarty. Let me say this also. Mr. Ribicoff said that he gave everyone carte blanche authority to give the committee any information it asked for, regardless of the budget that is before us. So I am asking you the questions, and you have all the leeway you want now if you could use that much more money.

Dr. Terry. Of course we could use it, sir, and use it to advantage, to the advantage of the programs and the American people, I think.

ENVIRONMENTAL HEALTH

Mr. Fogarty. And you mentioned environmental health in your prepared statement.

Dr. Terry. Yes, sir.

Mr. Fogarty. You are asking for an increase of $7 million. We held a 2-day hearing last year on the problems of environmental health, and I thought it was the Department's recommendation then that you could use about $25 or $28 million more. The Congress appropriated over $4 million more than the Bureau of the Budget allowed last year.

We thought we had some pretty good witnesses at that special hearing, and many of them wanted to go even higher than the Department's suggestion. But now you come in with a budget asking for $7 million more than we have this year. That is way lower than your witnesses suggested we could use a year ago.

Dr. Terry. Yes, sir; it is just a $7 million increase.

Mr. Fogarty. I am not going to press the question, because you have only been on the job a short time.

Dr. Terry. I have been on the job long enough, Mr. Chairman, to know that this is a very important part of our program. I have met already twice with the National Water Pollution Board, our advisory board. I have met with many individuals and with other groups representing interests in all of these areas of environmental health.

I must admit that this information that I have has been collected totally over the past 6 or 7 weeks, and naturally I did not, from the standpoint of my personal participation in it, have much to do with it, because I was not qualified at the time we had to make our suggestions for amendments, and I had nothing, of course, to do with the original submission of the budget.

Mr. Fogarty. I realize that. I am not pressing the question.

Dr. Terry. I think there is one point that I would like to make clear; that I think that this is one of the most important segments of our program in the Public Health Service, sir.

Mr. Fogarty. I do too, but the name "environmental health" does not ring a bell with most people. If you talk to the average person about environmental health, they say: "What the heck is that?"

If you talk to the average person about air pollution and water pollution and give them examples, they understand. Do you find that true?

Dr. Terry. Yes, sir.

Mr. Fogarty. I am talking about the lay people, of course.

Dr. Terry. Well, it is even a matter to understand among professional persons, and it has been a matter to the degree that we have been sufficiently aware of the problem that we have devoted a great deal of time and study trying to devise a better term, and actually we have not come up with a better term today. I think about the closest we can come to a conclusion on this subject at the present time is that this seems to be the best term that we can get, and if we are going to stick to this term, it is going to be necessary for us to do a good broad educational program in terms of letting the public and letting—even within the profession—people know what we are talking about when we speak of environmental health.

Mr. Fogarty. Who is going to defend the budget for environmental health?

Dr. Terry. Dr. Bob Anderson, who is the Deputy Chief of the Bureau and is heading up the program.

Mr. Fogarty. Well, we shall ask him about the details.

Dr. Terry. We have got a good program and a good man there, sir. I think we will go ahead.

Mr. Fogarty. Yes, I agree you have a good man. And I for one would like to see more money expended in this field. I have talked to a few people who think we ought to have another program like the Institutes of Health as far as the environmental health problem was concerned.

SEPARATION OF NIH FROM PHS

I asked the Secretary the other day, just off the cuff—I had not given the question any thought and I do not know what prompted me to ask it—but I will ask you the same question. Have you ever given any thought to divorcing the Institutes of Health from the Public Health Service, setting them up as a separate agency?

Dr. Terry. I have heard this matter discussed. I have personally not given any thought to it.

Mr. Fogarty. I have never heard it discussed. Has there been some discussion along this line?

Dr. Terry. As far as I am aware, not any official discussion, Mr. Chairman.

Mr. Fogarty. I see.

Dr. Terry. But there has been discussion among some of us with regard to it.

Mr. Fogarty. I see.

Dr. Terry. Generally speaking, the inclination I have obtained within the Service is a negative one toward the suggestion; in other words, feeling that this should continue as a part of the Public Health Service.

Mr. Fogarty. Would you have said that a year ago?

Dr. Terry. Yes, sir.

Mr. Fogarty. You would?

Dr. Terry. Absolutely; no question about it.

Mr. Fogarty. I had not heard of it before, and the Secretary apparently had not heard of it. It was just thrown out as a leading question to him the other day.

Dr. Terry. I do not know of any formal discussion of it, sir, or official discussion.

POLIO VACCINES

Mr. Fogarty. I understand you appeared before the legislative committee this morning.

Dr. Terry. Yes, sir.

Mr. FOGARTY. Was it about the problem of oral polio vaccine?

Dr. TERRY. Yes, sir. They were primarily interested in establishing for the record the status of the oral poliomyelitis vaccine and attempting to insure themselves of whether——

PROBLEMS ASSOCIATED WITH A LIVE VACCINE

Mr. FOGARTY. Can you, in a brief way, tell us what the problem is?

Dr. TERRY. Yes, sir; I can, and I will be happy to do so.

The problem with regard to the production of a live poliomyelitis vaccine is a complicated problem from the production standpoint. The attenuated virus, which is a virus which is not capable of producing the disease in man, has to be grown in tissue culture—monkey kidney, and allowed to grow and increase in numbers on this medium.

One of the problems has been, and one of the big complicating problems has been the presence of certain other viruses which are naturally present in the kidney tissue of monkeys which are apparently completely healthy. There are quite a number of these viruses that have already been identified, and we do not know how many more there may be that have not been identified. They are the so-called simian viruses.

These viruses, some of them do definitely produce antibodies when they are given to man, which would suggest that they are capable of producing disease. And actually, certain of them do, are capable of producing some disease in man. We do not know how much. But the conclusion has been reached by the Public Health Service, in association with our NIH and our Division of Biologics Standards—and our national advisory committee—that there is sufficient unknown about these viruses that one must set up standards for the production of a virus, which is to be used broadly, which will exclude these viruses. This greatly complicates the production of the vaccine as well as the testing of the vaccine before it can be released for use. And this is the thing that has slowed down considerably the production of the live poliomyelitis vaccine.

SALK VACCINE INOCULATION DRIVE

I think we are fortunate in this country in having the Salk vaccine available, which is highly effective when given in the recommended number of doses. But, of course, the distressing thing about it to us is that it requires four separate injections over a period of several months; and, consequently, in spite of all the big promotional and advertising type of programs that we put on with other health agencies, State and related health organizations, voluntary health organizations, and so forth, we still have a distressingly large number of our children particularly, but even young adults, who have not received an adequate amount of the Salk vaccine. As long as this condition obtains, we are in danger of serious outbreaks of poliomyelitis.

On the other hand, we know very well that we will not have any production—any significant supply of live polio vaccine available in this country until at least in the fall. Therefore, we do not have any protection in this toward the protection of persons during this coming polio season, which is largely during the late summer.

Therefore, we have, with the endorsement of the house of delegates of the American Medical Association, with the endorsement of our national advisory committee, we have started a program to publicize as widely as we can that live vaccine will not be available at least until next fall, and therefore that we should put on a big push to get as many of our people protected with the vaccine that we now have available as we can.

We have been in touch with all of the State and territorial health officers on this. We have been in touch with other health organizations, voluntary and otherwise, and we are attempting at this time to launch a program which will impress upon people: (1) that we will not have any live polio vaccine for the protection of the population of the country before this next polio season; and (2) that we have an effective vaccine, if it is given as recommended, in the Salk vaccine, and that we would urge as many people as possible who have not had the complete course to get it before that time, before the summer.

Mr. Fogarty. Well, it is a difficult problem to get people to go, is it not?

Dr. Terry. It certainly is.

RHODE ISLAND EPIDEMIC

Mr. Fogarty. The Salk vaccine was one of the great discoveries, and I thought that people would flock to these clinics and doctors to receive their vaccinations. But as you know, in Rhode Island last year I think we had one of the best records as far as inoculation was concerned, but we had the most severe epidemic in the country.

Dr. Terry. I am well aware of it.

Mr. Fogarty. Your Public Health Service sent some men up there, but there was not much they could do about it. As I understand it, the studies that they made might help this year, because they have received additional information. I think they did a really good job. They were good men.

Dr. Terry. Yes.

Mr. Fogarty. A couple of years ago the Legion did quite a job in some areas in sponsoring clinics.

Dr. Terry. Yes, they did.

Mr. Fogarty. In Rhode Island the Navy was very helpful during this past epidemic. A captain of the Navy had one of these "guns": what do you call it?

Dr. Terry. Hypospray.

Mr. Fogarty. Yes, hypospray. He could do, I do not know how many hundreds in a day, but it was far more than by conventional methods. But they also have difficulty in keeping it in working order.

Dr. Terry. One of my very good friends, Dr. Robert Hinkston, who is at Western Reserve in Cleveland, was one of the early developers of this gun, and they have had some technical difficulties, although he and his group have literally given hundreds of thousands of injections with it.

Mr. Fogarty. The Navy gave thousands in Rhode Island last year. But the people did not go until the epidemic struck.

Dr. TERRY. This is the distressing thing. You take now for the schoolchildren in this country, and with Salk vaccine available, the best information we can get is that 50 percent of them have not gotten a complete series.

MANDATORY VACCINATION

Mr. FOGARTY. What do you think of mandatory legislation at the State level that all children have inoculations before they enter school? It is a controversial question is it not?

Dr. TERRY. We are getting up, we think, over this country to 75, possibly to 80 percent overall already vaccinated; but it is this preschool area that any such law requiring vaccination before admission to school would not get that group at all. So that some other approach has to be made to it.

I think one of the most promising things in this direction has been that recently the polio vaccine has been incorporated with the other routine types of vaccinations given to children, such as the pertussis and other vaccinations given as an infant. And it can be given in this way. And if we can get our pediatricians on the ball, so to speak, and have them try to cover those areas, and then try to cover those areas where actually the children are not seen by pediatricians, I think it will give us our best opportunity.

There is one other thing that I would like to mention, if I may, sir.

Mr. FOGARTY. Surely.

SUPPLEMENTAL TO PURCHASE LIVE VACCINE

Dr. TERRY. In connection with polio, you probably saw in the paper where President Kennedy had recommended a supplementary appropriation of a million dollars to purchase live polio vaccine when it becomes available.

Mr. FOGARTY. Yes.

Dr. TERRY. This is to be kept as a reserve which will be used for studies in the control of epidemics. The evidence today indicates that oral polio vaccine, the Sabin type vaccine, when given within a few days, becomes effective in terms of the beginning appearance of antibodies. So that, in contrast to the Salk vaccine, which requires weeks to months, there is some protection within a few days, apparently, from the Sabin vaccine.

Therefore, it is entirely logical that, if you have a tool like this, you go into a community, you know that this is a type tool for whatever virus is in the community, to go in and carry out a study program, a field demonstration and investigation, in which you would give the live vaccine to all of the rest of the population or as large a percentage as you could, in an effort to contain the epidemic. Well, this is what this is intended for.

I think that there were two or three things that came out in newspaper articles about this announcement which were unfortunate. One was that it was said that the Public Health Service was going to accumulate and going to take all of the first vaccine that was produced. There was also a question in people's minds as to whether we were going to take the vaccine as it is now or was it going to be a product which was a licensable product. And the third thing was that we were placed in the position of having estimated what the cost of polio vaccine was going to be.

Well, with regards to those points, none of them was the intention of our group. In the first place, going to No. 3 first, the price of the vaccine, we asked for a million dollars in the hopes that we could buy 3 million doses or more with that. We have no more than a not-too-well-educated guess as to whether that is a reasonable estimate or not. Most of the people who are acquainted with this two-sided technique feel that we can produce it as cheaply, if not more cheaply, than the Salk vaccine. The Salk vaccine, in general, runs somewhere around 30 cents, insofar as production is concerned and injection of a shot. So that, using that as a figure, this statement was made.

The Public Health Service has not bought any vaccine. It will not buy any until we have licensed manufacturers who are turning out potent and, of course, safe products. And of course we shall not take all of the early supplies that are available in terms of making it available to all of the critical groups in the community.

We regret certain discussions that have resulted around this announcement, though at the same time we are very proud that the President has seen fit to endorse our need in this direction.

And I might mention, in this respect, a question that was asked this morning, was this a decision that we made after the blowout in the paper of 10 days or something around that, where someone, a physician—in the Journal of the American Medical Association—had expressed the opinion that the Salk vaccine was worthless or much of it was. This decision of ours was made long before this ever came out, and had nothing to do with that incident.

Insofar as that in concerned, we feel that this is the expression of an individual who is expressing his opinion. We feel that we have very strong evidence to the contrary.

And we feel that we have a reliable product which, in testing in the field and comparing vaccinated and nonvaccinated groups, demonstrates an efficiency of beyond 90 percent in individuals who have had all four of the injections.

Mr. FOGARTY. Were you able to satisfy those on the other committee?

Dr. TERRY. I do not know whether we satisfied them or not. I think the major concern, Mr. Chairman, which they registered was—well, this point was raised: Are the people who would manufacture the live vaccine the same people who are manufacturing Salk vaccine? And, in general, they are.

Well, the question then occurs to them: Would the fact that they have Salk vaccine in production now and on the market deter their interest in developing a live polio vaccine product?

We do not think that it would.

Other questions around the problem relate to many other things, like why we have not gotten ahead faster. We talked about millions of doses.

Mr. FOGARTY. Dr. Sabin has expressed that view on more than one occasion, has he not?

Dr. TERRY. Dr. Sabin has expressed many views which are contrary to ours and our advisory committee. But Dr. Sabin agrees that—he published in his article in one of the Sunday weekly supplements recently that, since we do not have a live vaccine, that we should push the Salk vaccine for protection for this season.

PRODUCTION OF A LIVE VACCINE

It is a problem of getting production. Dr. Sabin feels that it should have been pushed faster. Frankly, I do not know how the Public Health Service could have pushed it any faster.

Mr. FOGARTY. How many have applied?

Dr. TERRY. None.

Mr. FOGARTY. Why?

Dr. TERRY. For the simple reason that none of them is that close to production of a marketable preparation.

Mr. FOGARTY. I talked to some of them who say they are ready to start manufacturing it any time but they thought the standards were too strict. And another reason they gave was that they need some kind of insurance against another Cutter episode remote as the chance of that might be. But I do not think much progress was made there.

Dr. TERRY. Our General Counsel informs us that we have no legislation which would allow us to offer such protection at this time, and we have not asked for such legislation, sir.

Insofar as the standards are concerned, we realize that they are higher than they have been on any of the preparations that have been used thus far. On the other hand, I shudder to think of a repetition of the Cutter incident. And I think the best protection we have in that direction is that, when we come out with a vaccine, it is one that we know is not dangerous—not just think, but know.

Mr. FOGARTY. There are companies ready to start manufacturing?

Dr. TERRY. There are companies that are working on it and are producing some of it for experimental purposes now, yes, sir.

Mr. FOGARTY. Yes.

Dr. TERRY. The regulations—well, the guidelines, more or less the standards for the production of the vaccine have been published by the Public Health Service and furnished to the companies as long ago as last November. We expect to have by the end of the month the final standards which would be necessary in connection with licensing.

Mr. FOGARTY. Do you make these determinations on your own, or do you take into consideration the experience of these manufacturers?

Dr. TERRY. I certainly would not make it on my own. Personally, I would not be capable of doing it. We make it on the basis of getting the key people on our scientific staff, such as Dr. Murray.

Mr. FOGARTY. That is what I meant.

Dr. TERRY. With our Advisory Committee from the outside.

Mr. FOGARTY. Do you have the same Advisory Committee?

Dr. TERRY. Yes, sir.

Mr. FOGARTY. There have been no changes?

Dr. TERRY. No, sir.

Mr. FOGARTY. There were some complaints from some manufacturers that the Advisory Committee was stacked.

Dr. TERRY. I was not aware of that, sir. I do not think there is any justification for that. It is stacked in certain respects, inasmuch as you can find almost any individual viewpoint you want on the question of polio vaccine on that committee.

The amazing thing to me is that they, in meeting with the Surgeon General on January 23 and 24 in Atlanta, were able to come up with the series of concise, concrete recommendations as to what the Service should do, which I think is quite an accomplishment.

Mr. FOGARTY. Someone told me there was a lot of confusion at that meeting.

Dr. TERRY. I was not there, but I understand there was less confusion than at any meeting of any polio group that has ever been held.

Mr. FOGARTY. A lot of claims and counterclaims.

Dr. TERRY. Let me see; who was with you there, Dr. Bauer?

Dr. BAUER. Yes. There was the usual amount of filibustering on the floor; but when they actually got down to business, the recommendations were quite uniformly supported. I would not say unanimously, but most of them supported them.

PHS LEGISLATIVE PROGRAM

Mr. FOGARTY. You have quite a legislative program up here. How are you making out?

Dr. TERRY. I do not think we know yet, sir. About as far as we have gotten thus far is to get them into the hopper. We do not know how long they are going to grind yet.

Mr. FOGARTY. Do you think you are going to get a substantial part of the program out of these committees?

Dr. TERRY. I certainly do.

Mr. FOGARTY. Do you?

Dr. TERRY. Yes.

Mr. FOGARTY. Which ones?

Dr. TERRY. Oh, I think we are going to get practically everything we are asking for, sir.

Mr. FOGARTY. You think so?

Dr. TERRY. Yes, sir.

Mr. FOGARTY. You are more optimistic than I am.

Dr. TERRY. I think we will get aid to medical education. I think we will get help in the extension of our community facilities in terms of raising the ceiling on nursing home construction and other minor amendments to the Hill-Burton Act. I think we will get some water pollution legislation passed in time.

Mr. **Fogarty.** Yes; that has been passed before. That will likely be a relatively easy one to get through. But you have some tougher bills up here. What about medical care for the aging?

Dr. **Terry.** Everyone concedes that that is a tough one, and there are many, many viewpoints on it, sir.

Mr. **Fogarty.** Have you got the votes?

Dr. **Terry.** I do not have the least idea, sir.

AID TO MEDICAL SCHOOLS

Mr. **Fogarty.** What about direct aid to medical schools?

Dr. **Terry.** We have not asked direct aid to medical schools, except as a cost of medical education tied to this scholarship proposal.

You are talking about operating expenses?

Mr. **Fogarty.** Yes; operating expenses. How do you feel about it?

Dr. **Terry.** I personally feel that the schools need aid very, very badly, that we have schools that are in danger of folding if they do not get some assistance now. I feel that we have to get aid to them, regardless of how we do it; whether we go in the front door, side door, or back door, we have to get aid to them.

Mr. **Laird.** You are going in the side door and back door right now; are you not?

Dr. **Terry.** I am not sure, Mr. Laird, what you are referring to.

Mr. **Laird.** I would like to put a table in showing the amount of aid since 1951 that went through NIH to the medical schools, and this is exclusive of research grants and contracts which, of course, also help these schools considerably.

(Note.—For table indicating total aid, including research grants and contracts, see p. 54.)

(The table referred to above follows:)

Funds received by medical schools (research grants and contracts excepted)

Year	GRS-NIH	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Grants for construction of HRF	Total
1951		$2,055,000	$1,370,143	$654,854						$4,079,997
1952	$6,480	1,845,000	1,649,832	679,582	$1,080	$4,820		$2,106		4,188,900
1953	5,040	2,020,000	1,588,671	1,277,030	1,040	7,778		2,940		4,902,499
1954	7,500	2,145,000	1,509,119	2,182,828	750	12,146	$1,500	380,722		6,239,565
1955		2,015,000	1,546,949	1,934,265		64,329		855,250		6,415,793
1956	1,000	2,015,000	2,372,028	2,141,855		718,786		1,297,912		8,546,581
1957	8,500	2,982,000	5,260,608	3,126,124	37,000	1,632,622	1,500	2,598,778	$20.898,073	36,545,205
1958	1,431,763	2,898,600	5,936,995	4,036,999	39,750	1,871,526	405,666	3,033.444	12,363,321	32,018,064
1959	3,576,180	4,070,500	7,807,758	6,183,331	40,500	3,140.347	1.341,541	3,992,925	16,701,341	46,854,423
1960	8,222,306	5,436,915	10,148,644	7,422.953	158,520	5,857,588	2,436,623	6,605,547	13,464,852	59,753,948
1961 estimate	17,511,500	5,185,400	15,371,465	7,921,600	174,540	7,740,000	3,236,300	6,036,500	15,801,167	78,978,472
1962 estimate	17,261,500	5,185.400	10,763,014	7,516,364	200,200	7,740.000	3,569,300	6,036,500	15,000,000	73,272,278

Mr. FOGARTY. I was surprised to find out that so many medical schools really need help.

Dr. TERRY. Yes, sir.

Mr. FOGARTY. I was surprised when I visited the medical school at Harvard. I would not have thought before I visited them, that they would need much help. But I was hoping the administration would come up with some bill to give direct aid for the operation of the medical schools.

Dr. TERRY. Frankly, Mr. Chairman, if I may say so, I think we have a good proposal here. It is not all that we would like to do, it is not what the Association of American Medical Colleges has asked for, but I think it is a good proposal.

Mr. FOGARTY. I think it is a step in the right direction, but I do not think it is enough. I think we ought to go a lot further than we are going.

What about scholarships? Do you think you can get a scholarship bill through?

Dr. TERRY. I hope we can, sir.

Mr. FOGARTY. Do you think you have a good bill?

Dr. TERRY. Yes, sir; I think so.

CONSTRUCTION OF MEDICAL SCHOOLS

Mr. FOGARTY. What about the construction of medical schools?

Dr. TERRY. I think we have a good bill with respect to terms of Federal aid, with a two-thirds Federal matching for new school construction or expansion; that is, expansion which increases enrollment of existing schools.

Mr. FOGARTY. How many schools do you think would be built if you got this legislation?

Dr. TERRY. I do not know that I can make a guess on that. I know of at least 10 or 12 areas where they are literally on the brink. Now, which of those are going to take——

Mr. FOGARTY. You mean new schools or expansion?

Dr. TERRY. New schools, I was speaking of.

Mr. FOGARTY. Yes. That is only about 50 percent of the need, then; is it not?

Dr. TERRY. Yes, sir. Just about it.

But if we could get something like that started in the next 2 or 3 years, we will have made quite some progress, and particularly if we could get expansion of our existing schools.

Mr. FOGARTY. How many such medical schools do we have in the country?

Dr. LOWRY. Eighty-six.

Mr. FOGARTY. I have an idea that we may have one in Rhode Island soon.

Dr. TERRY. Next door at Connecticut they are too. Those are two areas that look quite promising.

Mr. FOGARTY. There would not be any hospital connected with this particular school, but they claim there are so many hospitals within a short distance of the school that they would not have to build a hospital.

Dr. TERRY. This is not an uncommon practice or pattern for a medical school—not to own or operate its own hospital but to utilize facilities, either State, city, county, or even too, in many instances, private institutions which are close by.

REORGANIZATION OF PHS

Mr. Fogarty. It has been brought to my attention that the President hardly mentioned the reorganization plans in his health message. Are you satisfied with the progress that is being made?

Dr. Terry. Yes, sir; I am satisfied with the progress that is being made. The only thing is that I wish that we could have gotten a bill through the last Congress, so that we could really have moved further ahead than we have been able to.

But as I mentioned here in my opening statement, there are quite a few things that we have been able to do within our existing administrative atuhority, and we have begun our lineup in that direction. I think we are making as much progress as can be made until the Congress gives us the authorization to create the bureaus.

CONSOLIDATION OF COMMUNITY SERVICE ACTIVITIES

Mr. Fogarty. I notice you followed the committee's suggestion and consolidated dental community service type of activities all in one place.

Dr. Terry. Yes, sir.

Mr. Fogarty. But somewhat the same situation has existed with respect to other categories, such as heart, cancer, mental health. Do you anticipate consolidating them in the next budget?

Dr. Terry. Consolidating heart and cancer field programs?

Mr. Fogarty. Yes.

Dr. Terry. No, we have them under a single heading insofar as the organizational structure is concerned—a division. But I personally feel that it is quite important to keep those separate in terms of these field demonstration and technical assistance programs.

Mr. Fogarty. How does the dental program work out?

Dr. Terry. Well, what we did was combine our program of dental public health and some related activities with our dental resources. And I think it is the general impression that this move was a good one.

Mr. Fogarty. I see.

Dr. Terry. I have not gotten into the details on it, sir, but it is the general impression that this was a good move and has served to consolidate many of our efforts and prevent some overlapping.

Mr. Fogarty. I notice in the Cancer Institute you have somewhat the same thing that we had in Dental. You have State control programs and community demonstration projects budgeted in the Cancer Institute. It would not work in Cancer?

Dr. Terry. We have all of the operations in Cancer of these programs moved downtown. The appropriation is like——

Mr. Fogarty. The budget is still the old way, though?

Dr. Terry. Yes, sir.

Mr. Fogarty. And you did change it in the dental program.

Dr. Terry. Yes, sir.

Frankly, Mr. Chairman, from my experience in the Heart Institute, I think it has had a very favorable influence to have this portion of our program which more correctly operates—our heart disease control program—which more correctly operates through our Bureau of State Services, supported through the Heart Institute in terms of the fact that there is a natural tendency to pull in the interests of our investigators and our people working in the other areas of heart disease to have more interest for more exchange across the line.

Mr. FOGARTY. Do you think the committee made a mistake in making this recommendation as far as the dental program is concerned?

Dr. TERRY. I do not know, sir. I have not studied it enough to know.

Mr. FOGARTY. Now it seems to me that much of the reorganization of the 1962 budget is in anticipation of Congress approving the Service's reorganization plans; is that right?

Dr. TERRY. Yes, sir; we do anticipate that Congress will approve it and we have presented it in a manner demonstrating how we will use it if Congress does approve it. On the other hand, sir, I think the reorganization is such that we are not dependent on this action by Congress and we can go ahead and make progress, even if Congress does not approve this section.

NEED FOR HIGHER PROFESSIONAL SALARIES

Mr. FOGARTY. What are you doing about getting the salaries raised?

Dr. TERRY. We have not done anything yet, sir.

Mr. FOGARTY. I think that is one of the most important things that you have to face. Do you agree?

Dr. TERRY. I certainly do. I say we have not made any specific recommendations. Dr. Shannon and I have had a conference with the Secretary on it. We have had some detailed staff studies on it.

Mr. FOGARTY. He thinks it is very important, as he said on Monday, and is going to try to do something about it.

Dr. TERRY. Well, I hope we have convinced him of that, because I think it is a question of whether we survive or—whether we survive as a fine organization or whether we regress to some stage of mediocrity.

Mr. FOGARTY. Well, we do not want that to happen.

Dr. TERRY. I do not either. I would like to get out when that happens, sir.

HISTORY OF 1962 BUDGET

Mr. FOGARTY. What did you ask for; what was your original budget to the Department?

Mr. KELLY. For the total Public Health Service?

Mr. FOGARTY. Yes.

Mr. KELLY. They had asked for $1,164 million against the $1,030 million which is included in the original President's budget.

Mr. FOGARTY. What did the Department do with that $1,164 million request?

Mr. KELLY. They recommended to the President $1,107 million.

Mr. FOGARTY. You mean you cut them down $57 million?

Mr. KELLY. Yes, sir.

Mr. FOGARTY. That is a considerable cut for the Public Health Service.

BUDGET AMENDMENT

Mr. **Kelly.** Then at Secretary Ribicoff's request, the Surgeon General submitted estimates to amend the budget of $1,030 million by $148,774,000.

Mr. **Fogarty.** Give me that again; at whose request?

Mr. **Kelly.** At Secretary Ribicoff's request, the Surgeon General suggested amendments to the budget of $148,774,000.

Mr. **Fogarty.** And what did Mr. Ribicoff do about that?

Mr. **Kelly.** He recommended to the President $147,382,000. And there are pending before you amendments totaling $80 million.

Mr. **Fogarty.** He only cut them about a million dollars, then?

Mr. **Kelly.** That is correct.

Mr. **Fogarty.** But the Bureau of the Budget did quite a job on you. What did you ask the Institutes of Health to be increased by?

Mr. **Kelly.** $101 million.

Mr. **Fogarty.** Did the Bureau of the Budget give any good reasons for cutting that $101 million down to $43 million?

Mr. **Kelly.** I think it was a decision by the President as to the amount of money in his total fiscal resources.

Mr. **Fogarty.** I thought you would probably ask for more than $101 million, Doctor. Is that all you could profitably use?

Dr. **Terry.** This figure was a result of considerable study. My staff and I carried out considerable study with Dr. Shannon and his staff, after I came into office; we felt that this would have given us what would be a fine operating budget for the National Institutes of Health for the coming year.

Mr. **Fogarty.** How does this compare with Mr. Jones' recommendation?

Dr. **Terry.** It compares very favorably with the Jones recommendation. It is above the Jones recommendation.

Mr. **Fogarty.** The Jones recommendation is a year old. What would you guess, if that committee got together again, that they would recommend for next year?

Dr. **Terry.** I would have no way of guessing that, sir.

Mr. **Fogarty.** Well, it would be a little more than what they recommended last year, would it not; would that not be a pretty good guess?

Dr. **Terry.** I would say, in general, that most of us feel that we are in a time and in an area of a need for expansion, gradual but definite expansion, of our research program.

Mr. **Fogarty.** This committee has always acted that way.

Dr. **Terry.** I know that, sir. I have no complaint about this committee either, sir.

Mr. **Fogarty.** We have always tried to give what we thought was just a good progressive program.

Dr. **Terry.** I do not think anyone in the Public Health Service is unaware of the very fine support we have gotten from this committee.

Mr. **Fogarty.** You were under some restraints, were you not, when you came up with only $101 million? Did you not have an overall ceiling of some kind that you had to work under?

Dr. **Terry.** Very frankly, I had not been given any figure by anybody above me, and this was the figure that we arrived at in discussions with the NIH, with the feeling that, after all, one must be realistic and face realistic fiscal responsibilities, and at the same time what we thought would allow us to advance our programs in a good fashion.

HOSPITAL CONSTRUCTION

Mr. Fogarty. I thought you would ask for the full authorization in hospital construction, though. I thought that was one of the most popular programs in the country, and the backlog of applications that you have is quite large.

Dr. Terry. This is one of our most popular programs. It was a question really in terms of the amount of support that was gotten there, the amount of—the job that had been done there, and increasing need in other fields, such as nursing homes and other facilities, where we needed to put the money, in trying to be realistic about dollars.

Mr. Laird. Along this line, Mr. Chairman, I notice that the Surgeon General said in his opening statement that the 1962 budget with the supplemental of an additional $35 million would provide for a speedup in these activities. How does this make for a speedup? This would seem to me to be the same budget level that you are operating under now.

Dr. Terry. In relation to hospital facilities construction?

Mr. Laird. Yes.

Dr. Terry. It is the same total budget.

Mr. Laird. How does that make for a speedup?

Dr. Terry. I think it makes for a speedup in terms of the increased facilities that would be made available in the nursing home and related areas.

Admittedly, some has been taken off the funds available for hospital construction under part C.

Mr. Laird. But it is the same level as this year, in total, is it not?

Dr. Terry. Yes, sir. I think it is exactly the same level.

Mr. Kelly. Yes.

Dr. Terry. Yes, sir.

Mr. Laird. My question is: How can this be referred to as a speedup? I thought that would give the impression that it was more than the current appropriation.

Dr. Terry. I think that that particular phrase that I used was intended to refer to all of the amendment requests. Yes; this was intended as an overall statement, Mr. Laird.

TOTAL DEMAND FOR FUNDS

Mr. Fogarty. If you funded all approvable applications the States have, how much could be used?

Mr. Kelly. We can submit it to the committee, Mr. Chairman, that survey by States.

Mr. Fogarty. All right.

Have you any idea what it is offhand? You can correct the figure anyhow.

Mr. Kelly. It is about $900 million, as I recall.

Mr. Fogarty. This is just about a drop in the bucket compared to the demand. I have just been given a table showing the figure I asked for. The Federal share would be $883 million. We are $700 million short.

Dr. TERRY. Rome was not built in a day, sir.

Mr. FOGARTY. I know.

Dr. TERRY. I realize it is short. I wish we had more money, too, sir.

Mr. FOGARTY. Is there any doubt in your mind about using it if the Congress gave you the $211 million authorized to be appropriated?

Dr. TERRY. There is not any doubt in my mind.

Mr. DORAN. Part of this $883 million is in the special categories where we are asking for all we are allowed under the ceiling.

ABSORPTION OF PAY COSTS

Mr. FOGARTY. What did the increase in pay costs amount to for the Public Health Service?

How much was absorbed?

Mr. DORAN. The total cost of the wage board and statutory pay increase, $9,576,000.

Mr. FOGARTY. How much did you absorb?

Mr. DORAN. $5,632,000.

Mr. FOGARTY. I understand the NIH absorbed all of theirs.

Mr. DORAN. That is right.

Mr. FOGARTY. How much did that amount to?

Mr. DORAN. I do not know offhand.

Mr. FOGARTY. Supply it for the record.

Mr. DORAN. About $3 million.

(The information requested is as follows: For fiscal year 1961 the National Institutes of Health absorbed increases in pay costs amounting to $3,067,000.)

UNFUNDED NIH RESEARCH GRANT APPLICATIONS

Mr. FOGARTY. How much will the NIH be short of having funds to finance approved applications for research grants?

Mr. KELLY. With respect to 1961, the tables show on the basis of the current apportionment, there will be $18 million worth of approved projects we cannot fund. We are now seeking to release the reserves at those Institutes where we have reserves, and there will be unfunded projects. We will have about $13 million worth of approved projects we will not be able to fund in 1961.

Mr. FOGARTY. What about 1962?

Dr. SHANNON. I do not have the figures with me.

ABSORPTION OF PAY COSTS

Mr. FOGARTY. Did you suggest a supplemental request for the pay costs?

Mr. KELLY. For the National Institutes of Health?

Mr. FOGARTY. The Institutes of Health and the Public Health Service generally.

Mr. KELLY. The amount of the request was the same as the estimate submitted by the Public Health Service. A decision which was made at the beginning of the fiscal year on a Government-wide basis, and on a departmentwide basis, which the Public Health Service had to adhere to, affected their determination.

There was a determination made that all agencies of the Federal Government, unless the Cabinet Officer were to make some special request of the President for exception, should reduce their yearend employment by 3 percent, and the savings that would result should be applied to a reduction in the funds for the pay cost. This was applied throughout the Department except in certain specific cases.

In the Public Health Service, they were specifically exempt in their direct medical care programs, hospital and medical care and the Indian health program. In the balance, they were required to reduce their yearend employment that could otherwise be financed by the 3 percent.

Mr. Fogarty. Do you figure we gave the NIH too much money?

Is that because you thought they had too much money?

Mr. Kelly. I do not think we took the position that any of the agencies had too much money. We took the position, with respect to the direct medical care programs, that the work was not deferrable, that the Service had shown that the direct medical care staff was not adequate to give a high quality of care and that they could not afford to reduce.

Mr. Fogarty. There is an $18 million backlog of approved applications and yet you make the NIH absorb all their pay cost. I do not understand that.

Mr. Kelly. When we began the fiscal year it was not apparent we would have $18 million or $13 million worth of approved projects not funded.

As a fact, we estimated $6,782,000 of the funds would not be required even after we gave account to the cost of the pay increase. We have subsequently revised that projection.

Mr. Fogarty. I believe Boisfeuillet Jones would have disagreed with you last year, would he not, according to the report they issued?

HEPATITIS

I noticed a newspaper story earlier this month that stated the Public Health Service reported that the number of cases of hepatitis for the week ending February 25 was the highest for any week since it was made a reportable disease in 1952.

Dr. Terry. Yes, sir.

Mr. Fogarty. Where did you have that particularly bad outbreak?

Dr. Terry. Around Pascagoula, Miss.

Mr. Fogarty. Is it under control?

Dr. Terry. Yes; everything seems to be under control there. All the evidence ties it to the consumption of raw oysters which were harvested from polluted areas. There was a break in the sewage disposal system there where the sewage was fed into a stream from which the oysters were harvested. Some had been harvested illegally. It extended into areas where there were legal oyster beds.

Mr. Fogarty. That is a problem in many places over the country.

We have oyster beds up my way. Every once in a while someone gets caught taking oysters in a polluted area.

What are you going to do about it?

Dr. Terry. One of the prime things to do in relation to this is to put as much emphasis as we can on pollution control measures. This of course is one of the most important measures in that direction.

Mr. FOGARTY. We have been doing a lot of talking about hepatitis for a long time. You are still not doing much about it, are you?

Dr. TERRY. I think we are doing everything we know to do, sir.

Mr. FOGARTY. Almost every year we hear about it increasing. The appropriation for it seems to remain almost the same.

Dr. TERRY. I think you would see a sharp increase in the appropriation recommendations if we had very specific measures to carry out to control it. I think we have to continue our research program in this area in terms of getting more basic information.

Mr. FOGARTY. How much are you spending on research now on hepatitis?

Dr. TERRY. I do not know.

Dr. SHANNON. I do not have a figure. It is definitely a disease of viral origin. But all the investigations in this country, both in the universities and commercial laboratories who have attempted to find ways and means of isolating it, have been unsuccessful at the present time.

Mr. FOGARTY. The incidence is increasing.

Dr. TERRY. Yes.

Mr. FOGARTY. It seems to me I read about it in the papers all the time.

Dr. TERRY. And it has been particularly bad this year.

Dr. SHANNON. The capability here is the limited number of leads that warrant being followed rather than the amount of support that could be thrown into the area where a breakthrough occurs.

FLUORIDATION

Mr. FOGARTY. Are you doing anything on the fluoridation program that you have not been doing in past years?

Dr. TERRY. Our plans are basically the same. Continued stimulation and technical assistance and related activities.

Mr. FOGARTY. I heard on the radio, or saw in the paper, that some nearby city reported on it after 8 years.

Dr. TERRY. It was Washington, D.C.

Mr. FOGARTY. The decrease in caries amounted to 60 percent.

Dr. TERRY. That was their estimation, on the basis of their survey of many thousands of persons. I think one of the most disappointing things to us in this whole field has been the extraneous issues which have been thrown into the question of fluoridation.

One is the violation of individual constitutional rights—giving one medicine whether one wants to take it or not.

The other is charges of the fact that this is a poison. It is a poison if given in sufficiently large quantities, but in the manner in which it is given to prevent dental caries in the fluoridation of water, there is no danger and no evidence to indicate there may be a danger in that respect.

One of the things that disturbed us a great deal was that of the municipalities. Where referendums came up during the November election, approximately two-thirds of them turned it down.

I think one of the things we have to do is to find out more about why people are taking this attitude and to try to find some effective way of getting our message across to the people.

Mr. Fogarty. Did you not have the same problem with chlorine years ago?

Dr. Terry. Yes, to an extent. I do not think it was ever quite to this degree.

Dr. Porterfield. Many of the same arguments prevailed when they attempted to chlorinate water, including the argument that this was socialized medicine.

Mr. Fogarty. I know. A lot of people with money get behind these programs and take full-page advertisements in newspapers and make quite a big campaign.

I think the dentists ought to educate the people a little better than they are doing. They could do more than they are doing in this area.

Are there many dentists, where it is not being put into the water supply systems, that use it topically? I do not seem to hear much about it.

Dr. Terry. I think it is being used to a fair extent in that direction.

Mr. Fogarty. What do you think about Crest toothpaste?

Dr. Terry. I know the American Dental Association has endorsed it as being an anticaries factor. It contains fluoride and all the evidence I have seen thus far, at least statistically, backs up the position the Dental Association has taken.

Mr. Fogarty. Then I understand someone is considering marketing a fluoride pill that can be put in orange juice.

Dr. Terry. I think those have already been available, not on any large scale, but have been available in the past. I doubt this will ever be a very effective way.

In the first place, all the evidence indicates the closer one gets back towards birth when fluoride is given, the more effective it is. The problem of continuous administration of tablets to infants, small children, and on the way up is a much more complicated procedure than if you are talking about convincing adults they should take fluoride tablets every morning at breakfast. I do not think it is a very encouraging approach, sir.

PROPOSED INSTITUTE FOR CHILDREN'S DISEASES

Mr. Fogarty. Do you think you will be sponsoring any legislation to set up a new institute for children's diseases?

Dr. Terry. We are expecting that we probably will.

Mr. Fogarty. Are you enthusiastic about it?

Dr. Terry. Yes, sir.

Mr. Fogarty. Are you?

Dr. Terry. Yes, sir.

I do not think it is a simple matter.

Mr. Fogarty. Some do not share your enthusiasm.

Dr. Terry. I do not think it is a simple matter; there are a great many problems associated with it.

Mr. Fogarty. We could without legislation do something to build up the Children's Bureau.

Dr. Terry. I have nothing to do with the Children's Bureau.

Mr. Fogarty. The Secretary could.

Dr. Terry. That is right.

I think it would be a real challenge, Mr. Chairman, in terms of the vertical sort of an arrangement we have in our disease categorical institutes, to have others created which in effect move across in a horizontal fashion with some components operating within that institute and some operating in the categorical disease institutes. It is going to take a lot of cleverness on the part of our administration at the National Institutes of Health to operate profitably under such a scheme, but I think it can be done.

INFANT MORTALITY

Mr. FOGARTY. The Children's Bureau points out in their justification that infant mortality varies by State from a low of 21.3 per 1,000 live births to 41 in the highest. I did not think there would be that much variation.

What is the reason for this? Is it lack of education?

Dr. TERRY. I think realistically enough, our highest infant mortality is among the low social, economic, and poorly educated groups. It is by far the highest there. There is a parallelism there. There almost certainly are many other factors of which I am not aware, Mr. Chairman.

Mr. FOGARTY. Every year more children than ever are being delivered in the hospital, not the home.

Dr. TERRY. That is right. For instance, here is one of the things we see in our Indian health program. We are getting now to where most of our Indian children are born in the hospital, and we find the morbidity and mortality rate for the children in the first 2 weeks of life is parallel to that of the rest of the American public. But whoops, at the beginning of the third or fourth week it starts going up. That is the time they leave the hospital and return home.

Mr. FOGARTY. Has the life expectancy of the Indian population gone up?

Dr. TERRY. Definitely.

Mr. FOGARTY. What is the life expectancy of an Indian?

Dr. LOWRY. About 45 years now.

Dr. TERRY. In the graph we have shown how well they correspond to the rest of the American population during the first few weeks of life, then it takes a sudden rise.

Dr. LOWRY. After they get home, many get sick and die after 30 days or so.

SUMMARIES OF VARIOUS PHS PROGRAMS

Mr. FOGARTY. Will you supply for the record what you are doing in the field of migrant labor, in the field of aging, juvenile delinquency, alcoholism, accident prevention, and improvement of nursing home care?

Dr. TERRY. We will be happy to do that.

(The information requested follows:)

SUMMARY OF NATIONAL INSTITUTES OF HEALTH (NIH) PROGRAMS IN AGING, 1960

INTRODUCTION

The purpose of this document is to report on the many programs in aging research being supported by the National Institutes of Health, including both intramural and extramural activities. There has been a notable increase in the number of aging research projects initiated during 1960 as compared with previous years.

The three broad areas in which research is being supported are the behavioral and social sciences, the clinical sciences, and the biological sciences. These research activities seek to provide the answers to questions relating to the older person's mental health, physical well-being, and the very basic questions relating to the exact nature of the biologic processes and their relationships with disease.

INTRAMURAL ACTIVITIES

It should be recognized that all NIH research projects will produce information accruing to the benefit of all age groups including the older age group. The research being carried on by the seven institutes in chronic disorders such as heart disease, cancer, arthritis, blindness, mental illness, and metabolic and dental disorders, all affect the older age group in varying degrees, as do the infectious diseases which also are the subject of constant study.

In addition, there are two intramural programs devoted especially to aging. These are the Section on Aging, National Institute of Mental Health, and the Gerontology Branch of the National Heart Institute.

1. Section on Aging, National Institute of Mental Health

This unit, established in 1953, is organized to secure, through experimental investigations of the behavioral capacities and physiological status of animals and humans, an understanding of aging as a natural phenomenon. It is attempting to accumulate systematic information concerning behavioral and physiological changes associated with age. In addition, it is systematically investigating age-related impairments of the mental processes in man and is studying possible methods of preventing or repairing such impairments.

This work is being carried out by a staff of psychologists, physiologists, and chemists working under the direction of Dr. James E. Birren.

Most of the deleterious behavioral effects of the aging process that have been demonstrated have been related to motor and reactive capacities. No evidence of degeneration of cortical or subcortical neural materials has as yet been detected. The observed deterioration in problem-solving performance in older subjects appears to be related to a detriment in associative facility and regulation, and much future research will be directed toward discovering ways of compensating for, repairing, or preventing some of the more distressing deficiencies of cognitive functioning associated with age.

The Institute's Laboratory of Clinical Science has been conducting a multidisciplinary investigation, assessing physiological, psychiatric, psychological, and sociological characteristics in a group of elderly symptom-free males. Findings indicate no reductions in cerebral blood flow and oxygen consumption as a result of chronological aging alone but associate such deterioration with arteriosclerosis of the cerebral vessels. In the psychiatric area, it was found that many of the psychiatric conditions are not age determined, but are similar to mental illness of other age groups, indicating that the aged mentally ill need much the same kinds of treatment as younger persons.

The subjects also cooperated in a sociological investigation. Answers were sought to such questions as: What are the activities, interests, and aspirations that make up day-to-day living? Do earlier patterns of living carry over into old age? How much of behavior is a function of current environmental circumstances? It was determined that there is a relationship between the loss of close relatives and friends and psychiatric assessments of depression and the subject's self-reported decline. Inadequate mental functioning was associated with poor social functioning.

A series of followup studies is planned in which survivors of the group originally studied during 1955–57 will be reevaluated to provide much-needed longitudinal data, bearing directly on the course of changes in various psychological functions during the very late years of life.

During the past year, the section on aging completed 11 of the 15 chapters planned for a monograph, to be published in the spring of 1961, which reports the results of the extended, interdisciplinary study of aging.

Members of the staff of the section on aging were called upon during the year to participate in a variety of extramural activities in the United States and abroad. Dr. James E. Birren, chief of the section, conducted a research seminar in the psychological aspects of aging and taught a graduate course on the cognitive function in old age at the University of Chicago. Dr. Birren also presented a paper before the Conference on the Physiology and Psychology of Aging in Paris, France. In addition to these activities, Dr. Birren served as organizer and chairman of the research seminar on psychological capacities held at Berkeley, Calif. This conference preceded a related conference, the Fifth International Congress of Gerontology. held in San Francisco, at which Dr. Birren acted as program chairman for the section on experimental psychology. Drs. Jack Botwinick and Edward A, Jerome also preesnted reports on their research at the Fifth International Congress of Gerontology.

At the conclusion of this report (app. A) is a complete list of professional articles and other written material which were published by the section during 1960.

2. *Gerontology Branch, National Heart Institute*

This unit established in 1941, is under the direction of Dr. Nathan W. Shock and is one of the oldest programs in the field of aging in the United States. The research being done ranges from studies of primitive forms of life to long-term studies on human beings of various age levels. Working with Dr. Shock are histologists, physiologists, biochemists, psychologists, biophysicists, embryologists, zoologists, chemists, and physicians.

The program of the branch is set up under two principal headings: Basic Biology, including the sections on Comparative and Cellular Physiology, Nutritional Biochemistry, Intermediary Metabolism, Morphology, Biophysics, and Molecular Biology; and Human Physiology and clinical Medicine, including the sections on Cardiocascular-renal Physiology, Metabolism and Endocrinology, Human Performance, Clinical Medicine, Psychological Aspects of Aging, Physiological Psychology, Mental Performance, and Personality.

Studies reported on during 1960 include longitudinal studies made on approximately 250 men age 18 to 100 years, from the upper socioeconomic and education levels living in the community. A few preliminary comparisons of measurements made on this selected sample with those made on an indigent population show that some physiological functions show differences, while others do not. For example, the sample group are, on the average, taller and heavier and show better retention of pulmonary function with increasing age than the indigent group. However, there were no systematic differences in basal metabolism or renal function.

A new equation for estimating body fat in the intact human from determinations of specific gravity or total water content, which introduces corrections for bond density (based on X-ray measurements) and muscle mass (based on creatinine excretion), was developed. Using this equation, a loss of body fat at advanced ages was found.

In another study on 200 subjects, no significant change with age was found in the protein bound iodine content of the blood.

Age changes in ability to perform simple motions efficiently have been studied using maximum back-and-forth swings of the arm. Measurements of excess oxygen required for the task have been made which permit the calculation of the efficiency of the motion at different amplitudes and rates of swing. It is apparent that age differences exist in the effectiveness of the mechanism controlling the movement.

Other studies indicated that age differences in speed of reaction are primarily associated with alterations in the central nervous system.

Short-term memory was more easily impaired in old subjects than young. This was true for both visual judgments of areas and estimates of time intervals. In the case of visual judgments, the age dependent interference was greater in subjects with low educational attainment than in those with high, but for the estimates of time intervals, both groups showed similar degrees of interference.

A mathematical analysis of mortality data has permitted a rational derivation of the Gompertz equation, with the identification of coefficients of the equation that can serve as an index of "vitality" in a population.

With increasing age, granules of insoluble material accumulate inside the cells of cardiac tissue in humans. The granules are highly fluorescent and can be observed microscopically in sections of cardiac tissue. The granules have been isolated from human hearts obtained at autopsy for chemical analysis. Preliminary results indicate that the particle is composed of lipid and protein.

The effects of environmental factors such as temperature, oxygen tension, and radiation on life span have been tested in fruit flies. At increased environmental temperatures longevity is substantially reduced. Exposure to 100 percent oxygen shortens and low oxygen (1–2 percent) lengthens life span in these flies.

These results lend support to the theory that the "rate of living" influences life span. High levels of radiation shorten life span of flies reared in sterile environments.

Age changes in tissue metabolism are being studied in liver, kidney, brain and muscle of young and senescent rats. Earlier experiments from this laboratory have shown that the activity of a proteolytic enzyme, cathepsin, increases with age.

In other experiments, using radioactive markers, it has been shown that mitochondria probably break down and are resynthesized as units. The half life of liver mitochondria was estimated as 10.3 days in both young and old rats.

Aging has also been studied in protozoan cultures (bleached *Euglena*) in which cell division has been halted by removing sources of either carbon or nitrogen from the culture medium. Cultures have been maintained at constant cell counts for 3–6 months. The cells remain viable, but the RNA content diminishes markedly with time. When the cells are "aged" in a medium that contains no sulfur they cannot survive for more than about 1 month. Thus the mechanisms which permit the cell to survive in the face of nitrogen or carbon depletion do not function in the case of sulfur depletion.

To carry out this extensive research program the Gerontology Branch utilizes the facilities of the Baltimore City hospitals which provide for laboratory space; a 50-bed research ward with all facilities for patient care; and access for study to all patients in the 1,500-bed hospital and 1,000-bed old people's home.

Preliminary plans for a new basic science research building, essential to relieve congested laboratory conditions at the Baltimore City hospitals, have been drawn up, with the assistance of members of the staff of the Gerontology Branch.

At the conclusion of this report (appendix B) is a complete list of articles and other written materials which were published by the branch during the past year.

EXTRAMURAL ACTIVITIES

Center for Aging Research

The center, established in the fall of 1956, is a branch of the Division of General Medical Sciences. The purpose of the center is to stimulate and assist the development of new research projects in gerontology at universities, medical centers and various other research institutions in this country and abroad; to maintain liaison between the NIH intramural and extramural programs, with other bureaus and divisions of the Department of Health, Education, and Welfare, and with other Federal agencies and organizations supporting programs in aging; to foster the training of additional research personnel; to collect and disseminate data related to research in aging; and to sponsor conferences, symposia, and seminars on research and training problems in the field of aging.

A major activity of the center is the identification of "gap" areas in aging research needing new or additional emphasis. A major basis in determining these "gap" areas is the information obtained through the yearly compilation of the document "Activities of the NIH in the Field of Gerontology." This publication lists all grants made by NIH for extramural as well as intramural research. The center classifies as relating to aging those projects concerned with changes that reflect time-related processes other than those instrumental in development and growth.

The activities of the center during 1960 included giving full cooperation to the White House Conference on Aging, working with the Federal Council on Aging, working with the Federal Aviation Agency with regard to its research grants program in the relationship between aging and pilot performance. assisting and attending many other national and international meetings on aging.

Fourteen major conferences with programs relating to the problems of aging were attended by the staff members during 1960. One of the more notable ones was the Fifth International Congress of Gerontology.

In line with fostering the exchange of information on aging among the countries of the world, the Center for Aging Research is sponsoring the publication of a translation, from the Russian, of the review by Prof. V. N. Nikitin, corresponding member of UKrSSR, Academy of Sciences, "Russian Studies on Age-associated Physiology, Biochemistry, and Morphology." This review covers Russian research in aging between 1761 and 1958. The Clinical Center Library translated the text, and the Russian scientific translation program translated the bibliography.

Other informational activities of the center include the preparation and distribution of Research Highlights in Aging, Summary of NIH Research Programs in Aging, and the Activities of the NIH in the Field of Gerontology. All booklets are available upon request to the Center for Aging Research.

A list of the speeches given and papers published by members of the CAR staff and other members of the Division of General Medical Sciences appears in appendix D at the conclusion of this report.

Expenditures for extramural research in aging sponsored by NIH have risen from $4,570,000 in 1958 to $16,234,564 in fiscal year 1960. It is anticipated that they will reach $20 million in 1961. Another million dollars is spent annually in the conduct of the intramural research program in aging.

Extramural projects have risen in number from 274 in 1958 to 700 in 1960, with a rise to over 800 anticipated for 1961. The projects listed by the Center for Aging Research represent that portion of the total number of submitted projects which specifically bears upon major problems of aging.

At the conclusion of this section are four tables covering the growth of the grant program in aging, reflecting the activity of each Institute and the Division of General Medical Sciences, since 1958.

Interdisciplinary Research Centers

In addition to the two previously established multidisciplinary programs at Duke University (1957) and Albert Einstein College of Medicine (1958), two new programs were approved and put into operation during calendar year 1960. These were Western Reserve University, Cleveland, Ohio, inaugurated May 1960; and the University of Miami School of Medicine, Coral Gables, Fla., inaugurated September 1960.

The program at Western Reserve University involves the entire university and several affiliated hospitals. Principal attention is being given to the chronic diseases, with emphasis on the rehabilitation aspects. Investigations into the basic biological changes in aging are also being carried out.

At the University of Miami School of Medicine the program will be entirely basic in its approach to aging. It involves the medical school, the main university, and the marine biology laboratory in related studies in anatomy, physiology, biochemistry, microbiology, and botany.

The program established at Duke University in 1957, has been most fruitful. Each year the number of research reports being presented by the Duke scientists is increasing. Some of the papers presented during 1960 are listed in appendix C.

The Duke program emphasises the psychiatric, psychologic, and social sciences. but also includes biochemical studies and studies on atherosclerosis.

The program at Albert Einstein College of Medicine is focusing on metabolic changes which result with aging, including research in the biochemical, physiological, and pathological alterations. Heart disease is receiving much attention, in addition to those genetic conditions which seem to predispose certain persons to illness.

Papers published by the scientists working at the Albert Einstein College of Medicine are listed in appendix C.

Program units

The Center for Aging Research and its consultants believe that more universitywide centers should be established, though in most cases not of the magnitude of those now in existence. These plans call for the organization and long term support of smaller program units in a number of institutions throughout the country. The objectives of such program units would be to provide a stable organization, an atmosphere of common purpose, and an intellectual and scientific environment for integration and concentration of effort focused on studies in aging.

Stimulation of research in the various departments of the institution would be a major function of these units. Periodic institutionwide seminars on the various aspects of aging would be conducted. Training opportunities would be developed and teaching activities would be fostered.

Division of General Medical Sciences

In its responsibility for supporting research and research training in the sciences basic to medicine and biology, and in public and environmental health and medical care, the Division of General Medical Sciences is carrying out a program primarily aimed at developing more information on the basic biological nature of the aging process in the cells and tissues of the body, in organs such as the liver, and as related to enzymes and hormones. The work includes investigations into the importance of genetics in the character of the aging process and in longevity. Studies on the influences of nutrition and on the effect of man's living and working environment also are being supported, along with investigation into better rehabilitation techniques for older persons. At present the division is supporting a total of 102 projects related to aging.

The Fifth International Congress of Gerontology held August 7–12, 1960, in San Francisco, was sponsored jointly by the Division of General Medical Sciences and the National Heart Institute. More than 1,100 persons representing 35 nations attended this meeting.

National Heart Institute

Effects of aging on human performance are intimately associated with effects of aging on the cardiovascular system since the activity of every organ in the body depends on an adequate supply of blood. The National Heart Institute, realizing that aging brings about major changes in the heart muscle and in blood vessels, pioneered in the conduct and support of gerontological research and continues to develop and sponsor programs of four types: integrated multidisciplinary projects; research in problems of aging; research in the care of the aged; and programs to train personnel and disseminate gerontologic information.

Gerontologic research conducted by the Institute constitutes one of the most comprehensive and longest established programs of scientific investigation into aging. This growing research activity provides a background of gerontologic knowledge and productive research studies that make it a national and international resource in the field.

Supporting aging research, 70 research and training projects classified as primarily concerned with aging are being currently supported by the National Heart Institute. Projects range from basic research on aging in short-lived lower organisms to integrated, cooperative studies of elderly persons. Scientists are investigating the influence on the aging process of diet, heredity, changes in hormone production, and changes in connective tissue, as well as the mechanisms of cardiac failure in persons over 65 years and the rehabilitation of elderly cardiovascular patients.

As previously reported in the section on the activities of the Division of General Medical Sciences (p. 13), the National Heart Institute shared in sponsoring the Fifth International Congress of Gerontology.

The National Heart Institute, working with the Atomic Energy Commission and the American Institute of Biological Sciences, continues to support research conferences on the relationship between radiation and aging. Reports of these conferences aid in the interchange on gerontologic information.

Three books have been published by an interuniversity committee, which was supported in part by the National Heart Institute. The first book, "Handbook of Aging and the Individual," was edited by Dr. James E. Birren; the second, "Handbook of Social Gerontology," was edited by Mr. Clark Tibbitts; and the third, "Aging in Western Societies," was edited by Dr. Ernest W. Burgess.

National Cancer Institute

Although the true relationship between cancer and the aging process is not known, there is reason to believe that the two may be closely connected. Scientists whose work is supported by grants from the National Cancer Institute are contributing information that could significantly increase knowledge of both malignant disease and the phenomenon of aging.

For example, it is generally accepted that our environment contains agents that probably contribute to the development of malignant disease. The fact that older persons have been exposed to such agents for relatively long periods may account for the greater occurrence of cancer in later life. Yet, it is also recognized that not all persons similarly exposed to environmental carcinogens develop malignant disease. Research in the area of environmental cancer will probably shed light on many important aspects of the aging process, including bodily changes that influence liability to malignant disease.

In other studies, scientists have observed that some mammalian cells growing in the test tube ultimately acquire malignant properties. Investigations in this area, which are concerned with the innermost workings of living matter, could provide vital basic knowledge of metabolic processes that are at the heart of the mechanism of aging, the cancer problem and perhaps all biological phenomena.

National Institute of Allergy and Infectious Diseases

This Institute is supporting a number of studies which are attempting to determine the interplay between age of the host and his susceptibility to infection. At the present time seven extramural studies are concerned primarily with problems in the field of aging.

National Institute of Arthritis and Metabolic Diseases

A considerable variety of studies on structural aspects and on physiological and biochemical aspects of aging are supported through research project grants by this Institute. Biophysical techniques, including electron microscopy and X-ray, are being used to delineate the fine molecular and tissue structure of senescent tissues, particularly in bones, joints, and endocrine glands. Investigations are also being made of alterations in thyroid and adrenal steroid function and of body composition in aging, of mineral metabolism in bone diseases afflicting the elderly, and of amino acid, vitamin and other nutritional requirements in relation to aging. Many fundamental studies performed by Institute grantees will provide information on growth, maturation, and degeneration in both single cells and whole organ systems. These include study of factors affecting the lifespan of red blood cells and of formation and deterioration of collagen, the chief constituent of articular cartilage and connective tissue.

Other Institute-supported studies are concerned with many aspects of diseases associated with aging, notably osteoarthritis and osteoporosis. Institute scientists at Bethesda are also investigating osteoporosis, osteoarthritis, processes of collagen formation and aspects of nutrition related to aging.

The Institute participates in the support of a comprehensive program of research in aging at the Yeshiva University's Albert Einstein College of Medicine.

National Institute of Dental Research

With an increasing population of middle-aged and older citizens, periodontal disease has moved to the forefront as a leading cause of tooth loss in this country. This is reflected in epidemiological studies by the Institute to determine the prevalence and severity of oral diseases.

Laboratory experiments have shown that tartar formation, a factor in periodontal disease, is not dependent on the presence of bacteria. Thus broad biochemical studies now being supported may provide the research leads necessary for an understanding of tartar formation and accompanying tissue changes.

Other basic studies seek to determine the extent to which bacterial endotoxins contribute to the degradation of oral soft tissues. Of particular interest are studies of bacterial enzymes that apparently play a role in the destruction of connective tissue necessary for the support and retention of teeth.

National Institute of Mental Health

Among those social problem areas which are of special concern to the National Institute of Mental Health, the subject of aging involves the greatest number of people. With the increasing complexity of society, the process of aging has become fraught with many mental health problems. The National Institute of Mental Health initiates, coordinates, and supports an extensive research grants program in the field of aging in an attempt to provide fuller understanding of the processes involved, to help alleviate the psychological problems of older people, and to restore to society some of the human potential now lost. The research projects on aging which the Institute supports bridge many disciplines and a wide variety of research approaches. Some of the biologically oriented studies are concentrated on the effect of aging on the central nervous system, senile degeneration of the brain, and cerebral physiology in functional disorders.

Other studies of the aging process relate to psychological criteria of aging, attitudes of older people toward death, general social attitudes toward old people, and environmental and personality factors influencing adjustment of older people, including a scientific investigation of adverse consequences of social isolation. Two large multidisciplinary research projects are concerned with the general aspects of the total aging process—physiological, psychological, and social. Another major study is concentrated on aspects of "normal" aging of older people living in an average community. During 1960 the Institute also supported a special research seminar on the social and psychological aspects of aging in order to promote wider exchange and utilization of new concepts in this field. However, despite research advances, and no matter what the hopes are for prevention of some of the adverse concomitants of old age, geriatric mental problems will continue to be a part of 20th century society. The Institute, therefore, is also supporting studies aimed at improving methods for care and treatment of psychiatric geriatric patients.

National Institute of Neurological Diseases and Blindness

Seventy-one extramural and several intramural projects are supported by this institute which relate directly to aging. Of prime interest are studies on changes in nerve cells and tissue function with age, particularly reflex action, cataracts, glaucoma, deafness, and strokes.

These studies have a special bearing on problems of aging and the state of being aged, since the nerve tissues and sensory structure of higher organisms play a controlling role in determining activity.

EXTRAMURAL STATISTICAL SUMMARIES

The following tables show the number and annual value of research and training grants in aging that were active on January 31, 1961, January 31, 1960, January 31, 1959, and January 31, 1958. The fiscal year columns indicate the appropriation from which funds were derived to support these projects. These tables essentially reflect calendar year activity. The date of January 31 was chosen in order to give full effect to the actions of the November meetings of the National Advisory Councils.

NIH research and training grants in aging, active as of Jan. 31, 1961

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1959	Fiscal year 1960	Fiscal year 1961	Total
General [1]	36	$83,288	$411,525	$912,662	$1,407,475
NCI	14		77,951	155,318	233,269
NHI	70	12,282	277,087	1,363,169	1,652,538
NIAID	7		12,217	45,446	57,663
NIAMD	47	14,220	169,665	605,382	789,267
NIDR	12		44,861	145,250	190,111
NIMH	31	83,038	420,483	479,662	983,183
NINDB	28		111,699	315,451	427,150
Total	245	192,828	1,525,488	4,022,340	5,740,656

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1959	Fiscal year 1960	Fiscal year 1961	Total
General [1]	66	$17,879	$713,503	$1,363,558	$2,094,940
NCI	47		384,588	510,335	894,923
NHI	149	94,410	1,166,600	2,457,291	3,718,301
NIAID	32	9,878	68,459	294,085	372,422
NIAMD	70		192,140	1,173,791	1,365,931
NIDR	24		133,637	256,626	390,263
NIMH	24		309,278	388,808	698,086
NINDB	43		156,319	802,723	959,042
Total	455	122,167	3,124,524	7,247,217	10,493,908

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[1] Division of General Medical Sciences.

NIH research and training grants in aging, active as of Jan. 31, 1960

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Fiscal year 1960	Total
General[1]	28		$393,851	$715,276	$1,109,127
NCI	19		82,449	279,697	362,146
NHI	72		316,365	1,400,322	1,716,687
NIAID	4		11,215	18,363	29,578
NIAMD	42		66,659	567,432	634,091
NIDR	19	$14,384	119,919	88,502	222,805
NIMH	31	72,678	485,141	461,129	1,018,948
NINDB	29		131,018	336,498	467,516
Total	244	87,062	1,606,617	3,867,219	5,560,898

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Fiscal year 1960	Total
General[1]	40		$171,519	$523,515	$695,034
NCI	38		211,577	469,738	681,315
NHI	117		907,711	1,792,053	2,699,764
NIAID	21	$18,384	42,811	192,825	254,020
NIAMD	49	11,129	104,670	888,129	1,003,928
NIDR	24	8,012	156,697	316,609	481,318
NIMH	20		190,189	228,416	418,605
NINDB	29		138,977	509,509	648,486
Total	338	37,525	1,924,151	4,920,794	6,882,470

[1] Division of General Medical Sciences.

NIH research and training grants in aging, active as of Jan. 31, 1959

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Total
General[1]	15	$18,192	$532,231	$550,423
NCI	20	120,021	424,407	544,428
NHI	60	227,888	1,034,709	1,262,597
NIAID	3	20,350	10,010	30,360
NIAMD	35	37,148	453,958	491,106
NIDR	11	38,785	60,774	99,559
NIMH	32	340,344	514,716	855,060
NINDB	21	109,706	190,741	300,447
Total	197	912,434	3,221,546	4,133,980

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Total
General[1]	14	$32,000	$268,910	$300,910
NCI	31	180,556	263,353	443,909
NHI	84	441,079	1,192,186	1,633,265
NIAID	10	24,833	81,558	106,391
NIAMD	32	50,344	528,042	578,386
NIDR	19	148,867	152,760	301,627
NIMH	6	43,499	53,397	96,896
NINDB	11	17,239	144,508	161,747
Total	207	938,417	2,684,714	3,623,131

[1] Division of General Medical Sciences.

NIH research and training grants in aging active as of Jan. 31, 1958

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1955	Fiscal year 1957	Fiscal year 1958	Total
General[1]	9		$12,258	$249,419	$261,677
NCI	11		40,853	99,991	140,844
NHI	48		138,700	747,329	886,029
NIAID	None				
NIAMD	14		41,179	132,434	173,613
NIDR	7		29,821	30,122	59,943
NIMH	28	$23,686	162,972	440,641	627,299
NINDB	14		37,751	79,215	116,966
Total	131	23,686	463,534	1,779,151	2,266,371
SECONDARILY RELATED TO AGING					
General[1]	5		$122,262	$81,951	$204,213
NCI	20		90,207	141,437	231,644
NHI	60		349,597	703,682	1,053,279
NIAID	7		2,501	60,574	63,075
NIAMD	21		82,181	192,470	274,651
NIDR	16		121,426	143,872	265,298
NIMH	6		38,298	35,706	74,004
NINDB	8		34,085	83,804	117,889
Total	143		840,557	1,443,496	2,284,053

[1] Division of Research Grants.

SPECIAL REPORT: JUVENILE DELINQUENCY[1]

EXTENT OF THE PROBLEM

Juvenile delinquency is a problem which merits the serious concern of the people of the United States. The number of delinquency cases disposed of by juvenile courts in the United States has arisen for 12 consecutive years. In fact, the number of such cases increased by more than three times between 1948 and 1959. And although the child population of delinquency age increased by about a third during this period, the actual delinquency rate per thousand children of delinquency age doubled. It is reliably estimated that one boy in five in this country has a delinquency record by the time he is 18 years old. It can, of course, be argued that many of the offenses that are counted in establishing this figure are relatively minor. This is true, but there are other reasons for regarding the official statistics as indicating only the part of the iceberg that shows above the surface. For example, it is reported by the Children's Bureau that for every child who becomes a juvenile court statistic there are two or three who are dealt with informally by the police even though they may have committed similar offenses. In addition, the Federal Bureau of Investigation indicates that for all reported major crimes in the United States only about one in four results in an arrest.

Looking in particular at offenses reported by the FBI in which youth figure prominently, it is observed that about half of all arrests for burglary and larceny involve persons under 18 years of age. Almost two-thirds of the arrests for auto theft involves such persons. Yet in these three categories of offenses slightly less than one in four result in an arrest. If juveniles commit a similar proportion of the offenses for which no arrest is made this would mean that the juvenile crime problem in these serious categories is more than double the size indicated by the official statistics. This fact cannot be minimized, since approximately half of all juvenile court offenses by boys are in the theft category. Boys constitute our major juvenile delinquency problem since they outnumber girls by about five to one in this regard.

But there are even more threatening considerations. Even if the delinquency rate levels off, the problem will increase by about 50 percent by 1980 since the child population of delinquency age will increase by about 50 percent in the next two decades. In addition, in the next decades many more of the people of the United States will be living in or near big cities. At present the big city delinquency and adult crime rates are at least three to four times the rural and smalltown rates. It seems likely, therefore, that as the Nation becomes more urban the delinquency and adult crime rates will continue to rise.

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[1] Prepared February 1961 as background information for the Director of the National Institute of Mental Health, Public Health Service, U.S. Department of Health, Education, and Welfare, in connection with fiscal year 1962 appropriations hearings.

It is true that when traffic offenses are excluded the national delinquency rate has appeared to be leveling off in the last 3 years. But one cannot tell whether this datum is encouraging until it is determined whether the proportion of recidivists and serious chronic offenders is continuing to increase despite the leveling-off rate. Also, the rate of traffic offenses is continuing to rise and certainly many traffic offenses constitute serious offenses against public safety.

THE REPORT TO CONGRESS

In view of this situation, in the spring of 1959, the House Appropriations Committee requested the National Institute of Mental Health to collaborate with the Children's Bureau in preparing a comprehensive report for the Congress on juvenile delinquency. The report was submitted in February 1960, and with its appendices constitutes a new source of documentation concerning delinquency. As a result of interest evidenced by both individuals and organizations, one of the appendices is currently being prepared for publication.

NEEDED TASKS

When the report was completed it was apparent that a number of needed tasks must be accomplished if adequate control of the problem is to be achieved.

(1) As indicated in the introduction, national data regarding the extent and nature of the problem is very inadequate at present. When a national rate increase is reported by the Children's Bureau this increase cannot be evaluated in terms of type of offense, proportion of chronic or recidivated delinquency involved, or segments of the juvenile population involved by socioeconomic status, ethnic group, age, family composition, etc. Given the present state of our knowledge, it is difficult to determine how seriously or in what ways such rate increases should be dealt with. If the increase is mainly in the area of minor traffic offenses and the mischievous behavior that is characteristic of adolescents the problem may not be one of national concern. If, on the other hand, the rate increase consists primarily of the more serious offenses as it is believed, and represents an increase in the chronic antisocial type of delinquent, the problem becomes very serious indeed, and requires much different control measures.

(2) It is important that demonstration projects be in operation to attack the problem at various stages of its development. Attention needs to be given to early prevention, to early identification of predicaments, to effective treatment of the first more serious offense, and finally, to the rehabilitation of the chronic offender.

(3) Because of the great shortage of trained personnel in the delinquency field it is important that training projects be inaugurated which develop and test training methods for all types of both professionals and nonprofessionals.

(4) Since there are no widely accepted techniques and instruments for evaluation of the effectiveness of delinquency programs there is need for the development of such instruments both for evaluating small programs aimed at a few individuals and for mass programs which attempt to deal with the problem on a citywide basis.

(5) Another high priority need is for a center in which research and service projects in the field can be described, cataloged, and made available to professionals and nonprofessionals in the field through journals, digests, collections of abstracts, series of monographs, films, etc.

(6) The foregoing needs must be met if the meaning of the problem for the United States is to be evaluated and so that immediate measures for attacking the problem can be undertaken. There is, however, a more systematic long-range approach which requires early inception. This is required because no experienced person in the delinquency field feels that adequate understanding exists at present regarding the processes which are involved in the development of the many different types of delinquents existing in our society. It is important, therefore, that mental health and social science theory relating to juvenile delinquency be structured into as coherent a whole as possible and then divided into areas or subunits which are amenable to scientific attack.

Once such areas are identified they can be carefully analyzed by groups of experienced professionals in the field so that appropriate research and demonstration projects can be applied to them.

(7) It is also important that collaboration with private effort in the field be sought, since such agencies as the Ford Foundation, the National Council on Crime and Delinquency, the National Council of Juvenile Court Judges, the American Public Welfare Association, the national police and juvenile police organizations, and others are actively concerned with the problem.

THE CURRENT INSTITUTE DELINQUENCY PROGRAM

Following the submission of the report to Congress, $1 million was earmarked in the 1961 Institute budget for new delinquency projects. This amount was allocated by the Institute as follows: $700,000 for demonstration projects, $200,000 for regular research grant projects, and $100,000 for training projects. In addition, an effort was made to see to it that the activities listed above which are deemed necessary for an effective attack on the problem be inaugurated as soon as possible. Much progress has already been made toward these objectives and it is anticipated that much more will be accomplished by the end of the year. The following accomplishments can be reported at this time:

(1) Pilot investigations are underway in three cities preparatory to undertaking a nationwide study of the extent, trends, and nature of the problem. In addition, negotiations are in process with a national survey organization regarding the conducting of a nationwide study.

(2) A number of demonstration projects are in operation involving approximately $570,000 in 1961 funds. In addition, it is estimated that as much as $600,000 in new grants may be approved for payment from 1961 funds before the end of the year.

(3) More than $100,000 has been allocated for training projects from 1961 funds and approximately $500,000 in applications are being reviewed.

Thus, it is anticipated that during 1961, funds in excess of $1 million will be utilized for new programs in juvenile delinquency.

(4) One large-scale evaluative instrument is being tested in New York City. In this project, valuable information regarding the extent and nature of the problem will be attained as well.

(5) An application for Institute support of a research and information center in the delinquency field has been approved this year.

(6) Theoretical conceptualization of the delinquency problem is being undertaken by Institute staff members, and groups of scientists and clinicians are being organized to consider various research areas in the field.

(7) Active liaison is being maintained with the Ford Foundation, the National Council on Crime and Delinquency, the National Council of Juvenile Court Judges, the American Public Welfare Association, the Council on Social Work Education, and other private agencies concerned with the problem.

Thus far the Institute has allocated over $3 million from 1961 funds for delinquency projects. Approximately $550,000 has gone to completely new projects, and it is estimated that another $700,000 in new projects will be approved for payment from 1961 funds.

In addition to projects centrally concerned with delinquency, there is a large number of others concerned either partially with delinquency or with problems which are highly relevant to our understanding of the problem. Institute staff members have analyzed and classified 108 projects into 11 categories which are either centrally concerned with or highly relevant to the delinquency problem. These categories include normal personality studies, studies of personality pathology, studies of family structure and processes, studies of peer groups, studies of the school and delinquency, studies of various preventive and treatment methods, studies of institutions for the treatment and rehabilitation of delinquents, studies of drug addiction and delinquency, long-term followup studies of delinquents, studies of special types of offenders such as sex offenders and runaways, and studies of multiple service communitywide attacks on delinquency.

SPECIAL REPORT: ALCOHOLISM [2]

INTRODUCTION

The field of alcoholism continues to be an important concern of the National Institute of Mental Health. The Institute's program in this field is designed to stimulate research, to raise the level of scientific inquiry, to aid in clarifying the uncertain knowledge which currently exists, to improve diagnostic and therapeutic techniques, and to provide consultation services to the States and other professional and lay groups interested in the problem.

Alcoholism is viewed by the Institute as a reaction to a series of stressful situations generated by a dynamic and complex interaction of physical, psychological, and social factors. The extent to which each of these factors contribute to the alcoholism syndrome is not now known. While the development of effective treatment and prevention techniques does not necessarily have to await the determination of the specific etiology of alcoholism, such determination will aid in reducing its incidence and prevalence. The Institute's program is, therefore, planned to acquire knowledge pertaining to the relationships among the physical, psychological, and social factors.

PROGRAM DEVELOPMENT

Four projects are of major importance in the Institute's program for research in the field of alcoholism. While these projects vary in content and method, the common underlying purpose is to meet a crucial need in the field: to clarify and evaluate existing knowledge. The projects are in various stages of development and no statements about their ultimate results can be made. However, it is likely that they will make important contributions to the understanding of alcoholism.

Cooperative commission on the study of alcoholism.—Members of the Institute's staff have been working with the North American Association of Alcoholism Programs (NAAAP) for the past several years in a combined effort to establish a cooperative commission which will have the responsibility for systematically reviewing and organizing the current state of knowledge in the field. Although the Institute and NAAAP have cooperated in the formation of the commission, it will function as an independent entity under a research grant from the Institute.

The major tasks of the cooperative commission, under the direction of a scientific director, are: (1) to make a comprehensive study of such scientific knowledge as now relates to alcohol use and alcoholism; (2) to inventory, study, and evaluate activities, programs, and resources now playing a significant part in attempts to solve or control the problems of alcoholism; (3) to investigate relationships between alcoholism organizations and other resources such as those in the fields of mental health, tuberculosis control, correction, and professional schools for the training of treatment and research personnel; (4) to use the results of these studies to formulate policies and recommendations for improving treatment, education and prevention, and (5) to identify in broad terms what further research is urgently needed.

Dr. Nevitt Sanford, professor of psychology at the University of California, and currently at the Center for Advanced Study in the Behavorial Sciences, Stanford University, has been appointed scientific director of the project. Though preliminary work is underway, the major program awaits the final constitution of the commission and the recruitment of the staff. The project will undertake a complete review and evaluation of the many facets of alcoholism. Several task forces will be formed to investigate specific areas. The scientific director will assume responsibility for the overall direction of the work which, in turn, will provide material for a major, long-term university study of problems related to the use of alcohol.

Alcohol usage patterns.—The purpose of this project is to develop instruments for gathering data about nonpathological alcohol consumption. It is essential that such data be gathered if a baseline from which to measure deviation in drinking patterns is to be established. This project is located in the Division of Alcoholic Rehabilitation of the California State Department of Public Health.

Influence of sociocultural factors.—It is known that social factors influence the drinking behavior of individuals; the extent and manner in which they are involved in the development of alcoholism is not known. The third project deals with the values and habits surrounding alcohol usage as they are affected by the cultural factors of various ethnic groups. This study is being conducted in Colorado.

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[2] Prepared February 1961 as background information for the Director of the National Institute of Mental Health, Public Health Service, U.S. Department of Health, Education, and Welfare, in connection with fiscal year 1962 appropriations hearings.

Nomenclature.—The fourth project is a nomenclature study. Its purpose is to clarify the confusing state of terminology in the alcoholism field. It will also recommend a nomenclature which can be integrated with the standard classified nomenclature of the AMA–APA and will be useful for research and treatment purposes.

RESEARCH

The investigations being supported by the Institute range from the specific drug effects of the ingestion of alcohol to the analysis of the complex social relationships involved in problem drinking. For example, some studies are concerned with the effects of chemical agents, including alcohol, cerebral oxidation and the manner in which alcohol is metabolized. Others are concentrating on the effects of alcohol on psychological processes. Sociological factors are also being investigated; one study is concerned with the behavior of the wives of alcoholics. Research support is also provided to investigators interested in the treatment and rehabilitation of the alcoholic.

PROFESSIONAL AND TECHNICAL ASSISTANCE

Consultation and technical assistance is provided to the States through the mental health consultants. In addition, technical assistance projects (TAP's) are also available to aid States in their alcoholism programs. These projects provide funds for workshops and conferences held in a specific State on a particular problem and have proven to be an effective mechanism for strengthening State alcoholism programs. Nine technical assistance projects were supported during 1961; last year eight States received such support. The following States have held TAP conferences during the current year: California, Colorado, Vermont, Kansas, Missouri, New Jersey, New Mexico, North Dakota, and Mississippi.

The Institute's Mental Health Study Center, continued its collaborative pilot project with the Prince Georges County (Md.) Health Department and is in the second year of a 4-year demonstration on public health approach to problems of alcoholism in the family. The project has three broad purposes—rehabilitation of the alcoholic and his or her family through the combined efforts of appropriate community facilities, development of an educational and preventive program, and evaluation.

Further attention and emphasis was given to alcoholism program activities already in several State departments of public health, some of which are State mental health authorities, and in some State mental health agencies other than State health departments. For example, State health departments in Kansas, South Dakota, and Wyoming, which are also State mental health authorities, make considerable use of technical assistance and consultation. At the same time, State alcoholism commissions and boards made use of similar assistance and consultation. They showed much interest also in developing closer collaboration with State health departments and with other State agencies. Thus, it is encouraging to note that the general trend of State alcoholism programs is to become more closely associated with State public health departments.

OVERVIEW

While progress is being made in the study of alcoholism, certain critical problems remain. These are the problems of the shortage of scientific personnel, the inadequate and inaccurate body of knowledge, and the generally low prestige of alcoholism as a field of study. These are not new problems and they must be solved if progress is to continue.

The Institute is concerned with the individual alcoholic as he functions within a social matrix. Thus, socioenvironmental and psychological factors assume equal importance with the physiological factor. The Institute's program has been developed to tap all three bodies of knowledge.

ACCIDENT PREVENTION ACTIVITIES

Funds	1960	1961	1962
Research grants	$1,125,265	$1,482,000	$1,921,000
Direct operations	401,400	1,440,300	1,447,000

The Public Health Service continues to take cognizance of the leading position of accidents among causes of death and disability. Ranking in fourth place among all major killers and in first place among killers of children above 1 year old and among young men and women through age 35, accidents exacted a toll of 92,080 deaths in 1959 and approximately 46 million injuries each year.

Although it is relatively new as a major activity of the Public Health Service, accident prevention can already demonstrate that by treating accidents as a major disease and applying traditional public-health methods, we can effect a substantial reduction in the accidental death rate and both the number and severity of accidental injuries. In organizing and pursuing its accident prevention activities, the Public Health Service has been careful neither to usurp nor to encroach upon areas either outside the reasonable scope of public health interest or now adequately pursued by other governmental or non-governmental agencies.

While the full impact of the economic costs of accidents, in terms of man-hours of productivity, might be considered outside the legitimate interest of the Public Health Service, the staggering medical costs are not. These costs are reflected in such statistics as, in 1 year: 38 million persons requiring medical care because of accidents; 11 million persons incurring accidental injuries requiring bed-time; 1,700,000 persons admitted to hospitals and utilizing millions of hours of scarce medical, nursing, and health technicians' time and a total of 50,000 hospital beds for an entire year.

It is interesting to note the comment of Governor Howard Pyle, president of National Safety Council, in the National Safety Council publication "Safety in the 1960's," that accidents in the decade 1950–60 cost the American people about $100 billion.

PROGRAM ACCOMPLISHMENTS

While specific accomplishments have been achieved in the brief career of the expanded PHS accident prevention program, the willingness of additional support on the part of many national, State, and local agencies, which heretofore have not participated actively in accident prevention activities, will have an even more profound effect on the success of accident prevention programs in the long run. It may be worth while to consider some of these at this time.

One of the most significant accomplishments is the increasing interest among State and local health departments in the application of public-health methods to the problem of accidents. While accidents are a major national problem, each accident is local; prevention, therefore, must also be local. The role of the Public Health Service must be one of ascertaining facts, defining problems, developing techniques, devising methods applicable over broad areas of the Nation, disseminating information, providing expert consultation, stimulating the upgrading of professional competence, and encouraging State and local health officials to recognize and assume their responsibilities for effective action. The extent to which State and local health departments have begun to undertake broad accident prevention programs is gratifying proof of the value of Public Health Service activity in this field. A total of 24 State health departments now report participation in some traffic safety activity; 41 States report activities in some aspect of family safety. Two States employ full-time personnel in traffic safety; 12 States report full-time personnel in family safety.

Similarly, the increasing interest of qualified scientists in the pursuit of basic, applied, and developmental research problems related to accident prevention is, to a great extent, a result of Public Health Service encouragement. Perhaps the greatest contribution the Service will be able to make toward the eventual diminution of the accident problem will be in stimulating imaginative and painstaking scientists and engineers to develop for us basic information that is so badly needed, and to devise methods of anticipating and overcoming human failings that make such a great contribution to accidents. Public Health Service grants for accident prevention research increased from $83,000 in 1956 to $1,125,000 in 1960.

A third general area in which at least a beginning has been made is in training. There is a great need at all levels of Government for physicians, nurses, and other health personnel with specialized accident prevention training. At present, this type of training is not readily available. Recognized educational institutions are being encouraged to establish both long and short courses tailored to the requirements of Federal, State, and local and privately financed accident prevention programs. Assistance is rendered to such institutions through advisers, lecturers, and the provision of resource material. The Service is now working with schools of public health to improve and extend the teaching and accident prevention.

Another significant contribution has been made in the long-needed effort to coordinate the activities of a great number of agencies, both public and private, working in the field of accident prevention. Some of these are interested in the broad spectrum of the problem, others in isolated segments thereof. Some are national in scope; others have only regional or local interests. Nevertheless, all are accumulating valuable experience and knowledge. A real effort is being made toward the evaluation, amalgamation, exchange, and application of the experience and findings of these heterogeneous groups. Through this coordinated approach many needs are being identified and joint courses of action are being agreed upon. Participation in efforts to coordinate accident prevention activities has been the practice of the Public Health Service in the interest of good management and economy.

Under the heading of specific accomplishments are a number of pilot projects which have already "paid off" in a visible reduction in injuries and which will continue to benefit the Nation as their findings are applied in wider areas.

One of these is a project in one county of Arkansas to which two Public Health Service representatives were assigned on a full-time basis. Here, as in many other areas of the South, fires were a leading cause of death and disability. Epidemiological investigation revealed that improper wiring of homes and improper use of coal oil accounted for a substantial number of the accidental deaths and injuries. There has already been a dramatic reduction in the human and property losses from fires, as a result of educational and other corrective measures instituted in the county.

A review of the data on persons hospitalized because of accidents in the Shenandoah Valley area indicates a reduction in the first year of about 20 percent in the incidence of injuries in the preschool child and young married adults. This would indicate that the family approach used was practical and can be applied in other rural areas.

A small pilot epidemiologic study of falls in elderly persons in Albany County, N.Y., suggested the hypothesis that broken hips from falls in elderly persons may in large part be due to a preexisting physical condition. This lead is being followed.

Following five regional conferences on the subject of drinking and driving, a national working conference on this subject will be held in May of 1961. An effort is being made to bring together all presently known facts on drinking drivers and pedestrians who have been associated with over 50 percent of vehicular deaths. These data will be assembled for use in developing and carrying out prevention programs.

A conference on simulation held February 27 through March 1, 1961, constituted the opening of a long-range effort to promote a better understanding of and the need for what may well be the most valuable single device ever developed in the campaign to reduce the death and injury rates on the Nation's highways through research. The form of the simulator has already been predicted in a feasibility study sponsored by the Public Health Service. Although many technical problems remain to be solved, these are now mainly of an engineering and developmental nature. When a simulator is built as the prototype of the several that are needed around the country, scientists will have a much more effective method for conducting research dealing with the many human factors that are involved in driving, without risking the lives of the drivers or others. The importance and value of this research device cannot be overestimated.

Prior to fiscal year 1961 major emphasis was directed toward the diagnosis and treatment of poisoning. Beginning in 1961, additional emphasis is being placed on the prevention of accidental poisoning. A pilot cooperative project to develop and test prevention measures and educational materials is being carried out in a local health department. Also, a medicine cabinet, developed by the Public Health Service, that is convenient for adult use but inoperable by small children is being considered by manufacturers for commercial production. Prevention of the serious consequences of lead poisoning in children is being approached through the testing of various early detection diagnostic methods to determine which is the most suitable for general screening use. The use of gastric lavage as treatment for accidental ingestions of kerosene has been evaluated. On the basis of these recent research efforts, it can be concluded that gastric lavage does not encourage the development of pulmonary complications as had been believed. There is indication that such treatment results in a reduction of pulmonary complications.

This, of course, can be only a quick sampling of the many avenues of accident prevention being explored by the Public Health Service and being exploited as rapidly and as thoroughly as available funds and manpower allow. The types of activities which, by research and application, can significantly reduce the accident toll in the future include, among others, encouragement of general proficiency in mouth-to-mouth resuscitation, improvement of safety standards for household appliances, epidemiological studies of motor vehicle deaths to identify preventable causative factors, and the development of criteria to determine who is capable of safely operating motor vehicles under modern traffic conditions.

Research grant funds

In the area of accident prevention, 29 research grants were supported in 1960. In 1961, continuing studies and new grants are expected to bring the total support to $1,482,000. The grants in these 2 years supported research at 14 universities, 4 State health departments, and 9 independent research organizations. These studies are all aimed at a reduction of the threat of accidents to public health—accidents, on the highway, in the home, at work, and at play—accidents which are responsible for an annual toll of more than 90,000 deaths and over 9 million disabling injuries. Some representative problems under study are:

Crash injuries in automobiles and aircraft.
Accidental poisoning.
Driving behavior and accidents.
Safety devices in cars.
Childhood accidents.
Adolescent driver characteristics.
Driver education.
School-age accidents and education.

It is anticipated that such research will uncover some of the basic causes of accidents and will permit the development of effective preventive measures.

ACTIVITIES UNDER THE GRANT TO THE INTERNATIONAL ASSOCIATION OF CHIEFS OF POLICE

The chief investigator, Mr. Robert Shumate, reports that even though it has been less than a year since the start of work under this grant, progress has been substantial, and two technical papers are in manuscript. An instrument has been developed which is actuated by an invisible tube on the highway and photographs each car going by and its location on the highway, and records its speed and the time. This information is recorded at the beginning and end of a sample segment of road, for each vehicle passing through. The information is fed into an IBM 650 computer through special programing developed under this grant. Out of it comes a continuous record of the traffic in this segment of road, including such phenomena as passing time, passing, headway, the formation of queues, and in short, the behavior of the entire traffic column.

The accident experience of the entire Wisconsin State road system for 3 years has been broken down into about 2,000 segments. A number of segments have been analyzed and the accident experience on them found to be consistent from year to year. Work is in progress in relating the accident experience in each segment of road to the traffic patterns as determined by the computer analysis. After this phase is completed, the investigators will attempt to develop enforcement patterns which will systematically change hazardous traffic patterns which tend to form on certain segments of the highways.

PROSPECTS FOR THE FUTURE

The action of Congress last year in appropriating additional funds for accident prevention work has had a salutary effect on the national effort in this field. More researchers are entering the field, more facets of the problem are being studied, and more vigorous action programs are being carried out. These efforts, however, will require additional encouragement and practical support before any lasting and measurable acceleration of the downward trends in accidental deaths and injuries can reasonably be expected. There is no doubt that a concentrated effort at identifying and correcting, eliminating, and compensating for the human failing which causes accidents will accelerate this downward trend. Emphasis must continue to be directed toward traffic, home, farm, and recreation accidents.

The economic losses due to accidental deaths and injuries, the human suffering entailed, and the tragic loss of lives among our youngest and potentially most productive citizens, all emphasize the need for constructive, preventive action, much of which is peculiarly within the experience and capabilities of the Public Health Service.

Under the new concept that "accidents don't happen; they are caused," public health agencies and all of the health professions are focusing their technical know-how and their humanitarian instincts on the solution of those accident problems which come within their professional purviews. Their efforts have already begun to make an impact on the accidental death and injury problem. What is more important is that they are beginning to identify additional areas that are amenable to public health treatment and to devise specific remedies for specific types of accident hazards.

Every new fact which is uncovered, in addition to providing new knowledge that can be brought to bear against accidents, serves also to increase our awareness of the vast amount of knowledge that is still needed and to point to new and important research that must be performed if the present high incidence of accidents is to be significantly reduced. The potential value of such research and the new information it will provide is evident in the figures cited above.

NURSING HOMES

In 1962 continued efforts will be made toward strengthening working relationships between hospitals and nursing homes and developing model record systems for nursing homes. In addition, effort will be directed toward organizing training courses for nursing home personnel in the care and rehabilitation of patients, improving nutritional services, and assisting State agencies in developing the kinds of programs that will help them to elevate the standards of care in nursing homes.

In carrying out these objectives work will be carried out with a variety of organizations: licensing agencies; welfare organizations; health departments; medical, nursing, and hospital authorities, as well as the nursing homes themselves and their national and State organizations.

MIGRANT HEALTH ACTIVITIES

A unit on rural health in the Division of Community Health Practice is the focal point for domestic migrant health interests in the Public Health Service. With the objective of facilitating and coordinating efforts to improve the health conditions of domestic agricultural migrant workers and families, the unit collects and analyzes data on agricultural migrant health problems and services, provides consultation to State and other agencies on migrant health conditions, cooperates in studies to improve migrant health services, and represents the Public Health Service on committees and in conferences with interested State and national groups.

MARINE HOSPITAL RESEARCH

Mr. Fogarty. Doctor, I have one final question. Do you intend to close any marine hospitals next year?

Dr. Terry. I have no plans and no intentions at the present time.

Mr. Fogarty. How about your research program? Is that progressing in these hospitals?

Dr. Terry. We are making progress, Mr. Chairman, but it is slow. We have gotten some very definite activities on the road, so to speak, and in several of our hospitals we have good research programs going. Much of it has been brought about by activities through the National

Institutes of Health in which we have taken some of our training funds which were available for training persons inside of the Service, and sending our young physicians out into the community. There is some training, you realize, but not in all the detailed research techniques and methodology. We are sending them out into the community where they are able to work in the medical schools, and after a year or two they are returned to the hospital to continue the working relationship with the persons under whom they have trained. This has been very effective. We have put some 18 of our physicians through this procedure.

Of course, the action of Congress last year which made our Public Health Service hospital physicians eligible to apply directly to the National Institutes of Health for research grants has already begun to show some progress. We have a few grants going there.

One of the most interesting of those grants is a large grant which has been set up as a collaborative and cooperative effort between several of our hospitals involved at the present time for a screening and study of the comparative value of well accepted and established drugs, and new drugs, to be used in the treatment of hypertension. It is a study similar to those that have been set up in the Veterans' Administration. So I think we are making some progress.

We have had problems, and we will continue to have some problems, but I think if we can continue in the direction we are going, and hopefully step it up some, we will begin to show real progress in the next 2 or 3 years.

Mr. Fogarty. Three or four years ago I made a trip down to Carville to see our hospital there. They convinced me that they needed some money for research in order to keep the doctors interested. How is that program working out? Is it paying off and are they satisfied?

Dr. Terry. I am really not acquainted with the details there and I would like Dr. Lowry to answer your question exactly.

Dr. Lowry. Yes. They initiated a research program and we were able to attract and keep some people. I would be pleased to have a summary of their accomplishments furnished to you.

Mr. Fogarty. All right. I wish you would, and put it in the record.

(The information requested follows:)

The research program at Carville is presently conducted by 9 full-time research workers financed from H. & M.C. funds appropriated for Carville research, 2 full-time workers financed from NIH grant funds, and 10 regular hospital employees who devote from 5 to 50 percent of their time to research. There are four general categories of study: (1) study of the clinical disease in its many diverse aspects; (2) study of the organism itself in regard to its metabolism, staining characteristics, reaction to drugs and chemicals, and its habits in human and animal tissue, efforts to culture the organism continue; (3) study of the response of both animals and human patients to new drugs; (4) study of the leprosy patients' environment, professional and public attitudes toward leprosy.

Specific projects underway include such activities as efforts to grow leprosy bacilli in embryomas; effects of lepromin in guinea pigs; the experimental treatment of leprosy with new drugs such as CIBA 1906, tapazole, etisul; the dye mechanisms of fuchsin and phenol on acid-fast bacteria.

Of special interest are studies of the effects of ultrasound on the course of leprosy; the search in living patients for evidence of amyloidosis, this study is of high prognostic significance; the promising effects of maleic anhydride in laboratory animals injected with murine leprosy; and finally the results of many years of study, now ready for publication, of the occurrence of transient opacification of corneal nerve fibers and pinpoint opacities which may involve the entire cornea, a condition pathognomic of and seen only in leprosy. Also of special interest are two projects in health education, one to study the attitudes of professional people toward the leprosy patient, the other to determine public attitudes toward leprosy.

Dr. Terry. There is one point I would like to make there, Mr. Chairman. You do not have to be in a remote, geographically isolated area such as Carville, La., to get this same attitude in your hospitals, where you do not have funds available to support research activities and when you have people who have good ideas and want to go ahead with them. It is one of the areas we have very seriously overlooked in the past in the Public Health Service, particularly the development of clinical research programs in our Public Health Service hospitals. I expect to do everything I can it stimulate it.

Mr. Fogarty. Thank you very much. I think you have done a very good job.

Dr. Terry. Thank you, sir.

Mr. Fogarty. Mr. Laird.

MEDICAL ECONOMICS

Mr. Laird. Dr. Terry, what plans do you have in the next year to study the area of medical economics?

Dr. Terry. I do not yet know the specific plans, Mr. Laird. We have some studies going on with relation to the availability of medical care, related to standards of hospitalization, of nursing homes, and that sort of thing, which is being developed in our Division of Public Health Methods. I haven't actually had an opportunity to get into what is being done there, except in a very general way.

Mr. Laird. It seems to me that in the Department of Health, Education, and Welfare, most of the studies along this line are done by the welfare people rather than the public health people. It would seem to me that the Public Health Service has some responsibility in this area.

Dr. Terry. I would certainly agree with you, sir. It is simply that I have not been in my job long enough really to know what is going on there.

Mr. Kelly. There is a new plan for this in this budget.

Dr. Terry. I think if Dr. Porterfield may address himself to that, he could give you a description of it.

Mr. Laird. All right. I would like to have a description of it.

Dr. Porterfield. Last year you may remember, Mr. Laird, in the appropriation we got a slight increase in salaries and expenses in the Office of the Surgeon General, which was used for the Division of Public Health Methods. Economic studies had been done previously as a part of other kinds of studies, but this was to begin a special study within the area of medical care administration; problems of standards of facilities and of services; the differences in utilization of different types of care under different situations, and of different populations, which would be a use, in part, of the statistics being collected by the National Health Survey. This has gone on this year somewhat more slowly than we would like, mainly because of difficulties of recruiting specialized personnel with this competence. However, in the last few months at least we have acquired the nucleus of a very excellent staff on this subject. They are beginning to conduct studies and have accomplished some, which I think, as you say, is quite late in the game compared to where we might have been, but which will give us a basis of objective studies on the problems of medical care administration and utilization and efficiency.

I might say in this respect that in very recent weeks as the various elements of the Social Security Administration have been working on the one hand with the medical assistance to the aged, and on the other hand with considerations of the problems attendant upon the health insurance for the aged proposal, the Division of Public Health Methods and this unit is being utilized as consultants and as experts to provide this kind of intelligence for these programs; and while we would not propose to enter into competition with social security and the welfare kind of studies, nevertheless with respect to medical care, we think that there is a considerable area we have covered from the point of view of distribution, and quality, and quantity of care needed and used in the country.

EFFECT OF INSURANCE PROGRAMS

Mr. LAIRD. I think that there is an area of medical costs that has not been studied adequately. I mention the effect of the insurance programs which we have built up over the past few years, and which have grown at an amazing rate. It seems to me we have not had a real study of the effects of these insurance programs on medical costs, and certainly medical costs have been affected by it.

Dr. PORTERFIELD. That is right, sir.

Mr. LAIRD. But where do you go for the answers?

Dr. PORTERFIELD. Well, there has been an agreement within the Department very recently as to a division of responsibility on the score of where do you go for these kinds of answers, and who shall develop this competence. I think our budget reflects to some degree for 1962 an effort to meet this responsibility.

Mr. DORAN. There is an increase proposed of $95,000 for 1962.

Mr. LAIRD. The increase you have allocated for this type of study in your 1962 budget is $95,000?

Mr. DORAN. About $95,000.

Mr. LAIRD. What is the total amount that will be available in 1962?

Mr. DORAN. There was an increase of $100,000 for 1961.

Dr. PORTERFIELD. It would be on the order of $200,000 identifiable for this specific purpose.

PHS RELATIONSHIP TO MEDICAL CARE FOR AGED PROGRAM

Mr. LAIRD. The legislation sponsored by Senator Kerr and Congressman Mills—which has become known as the Kerr-Mills medical care program for the aged—as it passed the Congress, made no provisions as to who would handle it in the Department of Health, Education, and Welfare. It seemed to me that the Public Health Service should have had the responsibility. I made certain presentations at the time to Dr. Burney and to the Secretary of Health, Education, and Welfare, and I was advised that the Public Health Service was not in a position to handle that kind of medical care program. Why isn't the Public Health Service in a position to do that?

Dr. PORTERFIELD. Well, if I understand the question to which you got the answer you just quoted, the Public Health Service was not felt to be in a position to handle the relationships with all of the State agencies, which are in the main welfare agencies, where the money paid is through welfare channels as a Federal administrative agency. This the Bureau of Public Assistance in the Social Security Administration has done previously, and it is doing under the medical assistance to the aged legislation.

Mr. LAIRD. That was not provided for in the legislation, though?

Dr. PORTERFIELD. Not specifically. No, sir.

Mr. LAIRD. That determination was left to your Department to make?

Dr. PORTERFIELD. To the Secretary.

Mr. LAIRD. Did the Public Health Service make any presentation to the Secretary at the time that this decision was made?

Dr. PORTERFIELD. Yes, sir. We were in on discussions with Secretary Flemming and have had at least one conference, preliminary in nature, with Secretary Ribicoff. At the same time, negotiations have been going on at the staff level with the Bureau of Public Assistance, whereby we expect to provide it this kind of expertise in the methods of administering medical care, the efficiencies and savings which may result, and the quality of services to be given or paid for, which I think will be successful.

We hope, although we cannot assure this yet, that this will include not only a unit in headquarters here for economic studies, but it can also include some people in our regional offices to provide technical assistance to the actual administrators of the public assistance program in this field of medical quality.

Mr. LAIRD. I do not like to let this program get identified with public assistance. I think everything is being done in the Department of Health, Education, and Welfare at the present time to get the program into that particular area, rather than to treat it as a medical care program for the aged. This was not set up as a welfare program.

Dr. PORTERFIELD. I can only answer that again, that since most of this payment for service is carried on presently under the public assistance program and through welfare departments in States, that this was the decision made last year. On the question of review of this decision and a better way of doing it, I would have to look to the Department.

HOSPITAL COSTS

Mr. LAIRD. I note that hospital costs in the United States have gone up again this last year for about the 14th straight year. Do you see any indication that hospital costs may be reaching some sort of a plateau? I believe there has been about a 50-percent increase since 1945.

Dr. PORTERFIELD. Personally I do not know of any indications yet that we have reached a plateau in the increase in hospital prices. It is quite true that they have gone up steadily, for several reasons. One is the increase primarily in labor cost of the hospital; and, secondarily, it is in the increased technicalities of providing hospital services—the types of expensive equipment and the expense of specialized services which are expected of a hospital now, in contrast to older times when these were not available. I think perhaps in terms of unit cost to the patient for illness, that the increase in hospital cost has not been as great because what has been an increase in per diem costs has been offset by the average shorter stays of anybody who goes to the hospital, or of people with a given kind of illness. Where the per diem might have been double what it was 20 years ago, the time that a person stays in the hospital will be halved, so that he is actually not paying a great deal more for his hospital bill per stay than he might have in the older days. Also, he runs a higher percentage chance of getting out alive now than he used to, rather than through the back door.

We have and are continuing to carry out studies not only in this unit I have described, but in the Division of Hospital and Medical Facilities, the Division that administers the Hill-Burton program, which, as you know, has a section authorizing some activities in research in hospital administration. Some studies are going on in this area to identify the reasons for costs and the improvement of efficiency.

In effect, and not to give you too short an answer today on this, much of our effort today is geared toward attempting to steer the patient who does not require the full strength of hospital care into a lesser type of care more commensurate with his particular needs. This is done in two ways: One is to foster the idea of progressive patient care in a hospital where you provide in certain parts of the hospital highly intensive care and all types of technical and personnel services that the acutely ill need; and provide other parts of the hospital with lesser degrees of care, even down to an ambulatory ward where the patient dresses himself and cares for himself in general, and goes to his own meals in a central eating facility, and is in the hospital to be closely available to the diagnostic and therapeutic resources.

The second attempt is to follow this progressive patient care concept outside of the hospital, and to urge that the patients be discharged from the acute general hospital to a nursing home, or to a convalescent hospital, or to a halfway house type of facility, which has all of the services he needs at that stage of his illness, but not so many as the general hospital provides for the more acutely ill patients. This goes down even to the promotion of health care programs in the home, which is the cheapest of all for those people who can get along in their own homes with certain special types of assistance in the way of nursing visits, or homemaker care, or specialists of one kind or another.

We are seeing a fair amount of success in this, but of course nothing like the size of the problem in this country. People are still enamored of the idea of the general hospital as the perfect solution. We are far behind in the provision of high quality nursing homes. Many times people are kept in the general hospital because there is no nursing home to which they may be sent.

As far as home health care programs are concerned, these are available in very few communities of the United States today, and we would like very much to promote their use in many more communities, because they are effective when established.

Mr. Laird. Dr. Terry, we will go into that in a little more detail when the hospital people are up here on the Hill-Burton program.

Dr. Terry. All right.

IMPROVEMENTS NEEDED TO STRENGTHEN RESEARCH

Mr. Laird. I would like to find out what your thinking is, Dr. Terry, on the elements that are necessary to improve our medical research program. What are we lacking? Is it facilities, manpower, funds, or what is it?

Dr. Terry. Frankly, Mr. Laird, I do not think there is any one area you could point out as being the one, or even being the outstanding one. I think some of our very great needs that are remaining today are in facilities. We certainly need an expansion of our research facilities. Much of our research that is being conducted in this country today is being done in adaptations of previously existing space that is not at all economical in terms of the person's time, and actually to some extent it even on occasions influences the actual outcome of the investigation. So that there is no question in my mind but that we do need an increase in the facilities which are available to support medical research.

FEDERAL GRANTS FOR MEDICAL RESEARCH FACILITIES

Mr. Laird. Why is it, Dr. Terry, that there is no request in this budget, either in the budget amendment or the original budget, for grants to construct research facilities on a nonmatching basis?

Dr. Terry. I think we are primarily influenced in this direction, Mr. Laird, by the fact that although we realize that there are existing circumstances where it is difficult for persons and groups to raise funds locally, it is an awfully hard bill of goods to sell on a nonmatching basis when we have as large a backlog as we do of approved grants on a matching basis that we do not have the funds to pay.

Mr. Laird. Is it not true, though, that some of the unfunded applications on a nonmatching basis have a much higher priority than many of those on a matching basis?

Dr. Terry. I do not know of an adequate evaluation of that, and whether Dr. Shannon does or not I am not sure.

Mr. Laird. Would it not stand to reason that there are institutions that are unable to participate under the matching provisions of the Medical Research Facilities Act?

Dr. Terry. Yes, sir. I think so. I do not know the magnitude, nor the importance of that.

Mr. Laird. This committee started a program last year under section 433(a) of the Public Health Service Act, in which I understand that the applications are running about $5 of requests for every $1 that you have available.

Dr. Terry. I think that is correct, sir.

Mr. Laird. These are all research facilities requests which cannot participate under the matching program because the institutions do not have even the 50 percent to put up to meet the requirements of that program. I was rather disappointed that the Public Health Service did not look with favor on the program, and I note in your request to the Department you did not include any funds for this type of an approach.

Dr. Terry. That is right, sir. We did not.

Mr. LAIRD. Why was that decision made by the Public Health Service?

Dr. TERRY. I suppose largely on the basis, Mr. Laird, that we were giving first priority to those who could do something on their own, in effect.

Mr. LAIRD. Did you give consideration to need?

Dr. TERRY. I do not know how well that need was evaluated, sir.

Mr. LAIRD. There must have been some study given to this, though. I realized that you have only been in office for 6 or 7 weeks, and I am not trying to embarrass you in any way, but you did have something to do with drawing up the budget for the Heart Institute.

Dr. TERRY. That is right, sir.

Mr. LAIRD. And we noticed that the Heart Institute gave no consideration to it. The Cancer Institute did not give any consideration to it. I am rather disappointed. There must be some reason why consideration was not given to it.

Dr. TERRY. I think realistically in connection with the discussions that took place on the floor of the Senate last year when Senator Hill presented this to the Senate and he said this was a one-time basis, indicated that he would not——

Mr. LAIRD. I did not see anyone join with Senator Hill in that discussion on the floor of the Senate.

Dr. TERRY. As I recall it, no one disputed it either, sir.

Mr. LAIRD. I wasn't in the Senate Chamber at the time but I did notice in the Record that no one either disputed or agreed with anything he said in his rather lengthy presentation. The presiding officer put the standard question on passage of the report and amendments and then the Senate went on to other business. So this is a pretty thin reason for stopping as important a program as this.

Have you had an opportunity, or has anyone in the Public Health Service had an opportunity to talk with some of the deans of the medical schools around the country, that are carrying on medical research, to hear about the crying need for facilities that exists in this country today?

Dr. TERRY. Oh, yes. We have talked many, many, times with them, and many of us have done so, sir.

There is no question about the need for facilities.

Mr. LAIRD. I found in my discussions, universally, that that has been one of the first things that is called to my attention throughout this country.

Dr. TERRY. Mine too, sir.

Mr. LAIRD. That is, that facilities are lacking to carry on a proper program.

FUNDS RECEIVED BY MEDICAL SCHOOLS FROM NIH

Earlier today I submitted a chart that showed the amount of help that the National Institute of Health are presently making available in the area of medical education. That chart was exclusive of research grants and contracts.

I would like supplied at this point in the record a chart which includes research grants and contracts to the various medical schools.

(The chart referred to follows:)

FUNDS RECEIVED BY MEDICAL SCHOOLS

[In thousands]

Year	Research grants	Research contracts	Other [1]	Total	Grants to hospitals, principal investigators affiliated with medical schools
1951	$9,310	------------	$4,080	$13,390	($1,598)
1952	11,678	------------	4,189	15,867	(2,371)
1953	12,609	------------	4,902	17,511	(2,255)
1954	16,753	6	6,240	22,999	(3,402)
1955	19,496	------------	6,416	25,912	(3,849)
1956	21,769	52	8,547	30,368	(4,701)
1957	40,459	28	36,545	77,032	(9,571)
1958	50,343	106	32,018	82,467	(9,905)
1959	67,818	135	46,854	114,807	(13,585)
1960	93,297	197	59,754	153,248	(19,255)
1961 estimate	147,000	183	78,978	226,161	(28,000)
1962 estimate	170,000	185	73,272	243,457	(32,000)

[1] Includes grants for construction of health research facilities from 1957 through 1962, training grants, supply grants, and schools of osteopathy.

Mr. LAIRD. I have often heard it said that the majority of the medical schools in this country would have to shut their doors if it were not for the Federal aid that they were already receiving. Do you think that that is probably a true statement?

Dr. TERRY. I think it has been of a great deal of help to them, sir. Whether they would have to shut their doors or not, I cannot answer that; but I think that the assistance that has been given has been a great deal of help, particularly in the category of undergraduate teaching grants, the supplying of funds for personnel who have spent a large part of their time in research, but who are also available for teaching to some extent, and in many other ways. There is no question but that we have rendered a tremendous amount of support to the medical schools.

Mr. LAIRD. This is often referred to as side-door or back-door aid.

Dr. TERRY. Yes, sir.

Mr. LAIRD. Do you think that the front-door approach will replace the side-door and back-door approach in helping these medical schools?

Dr. TERRY. I think it will evolve. Yes, sir. I do not know how long it will take.

Mr. LAIRD. Are you thinking in terms of making a direct cash grant and letting the medical school make the determination rather than earmarking it, as we are doing it now?

Dr. TERRY. That was the general type of support I was referring to when I said that I thought it would evolve.

Mr. LAIRD. Do you envision that taking the place of this other approach we are currently using?

Dr. TERRY. I suspect that they will both continue to an extent, Mr. Laird. The actual worth of much of the so-called side-door support that we have given thus far is hard to evaluate. In other words, if a person is supported on a research grant in an institution and does part-time teaching, it is very difficult to place an exact monetary value on what this is worth to the school. I think that frankly many of our researchers are better off for doing teaching too. So that I would not like to discuss that development at all. I think that the major thing we have been interested in is that thus far—and I would want to continue this attitude—that persons who are suppored on the basis of doing research should have at least a very large proportion, and commonly we think in terms of 90 percent or so, of their time being used in that direction.

CONGRESSIONAL EARMARKING OF RESEARCH FUNDS

Mr. LAIRD. What is your attitude, Dr. Terry, to Congress earmarking research funds for particular types of medical research activities?

Dr. TERRY. I have mixed emotions on it. At times I think it has definitely been helpful in stimulating us to go out and seek areas of support outside of the particular areas for which the funds have been earmarked. On the other hand, I think at times it has been a distinct disadvantage insofar as operating our overall research program is concerned, because as much as we are stimulated and as much work as we did for particularly earmarked funds, we could not invest it all well in that area.

Mr. LAIRD. I am in the same position after listening to your answer as I was before I asked the question. I still do not know what your opinion is with regard to earmarking funds. You feel sometimes it is all right and sometimes it is not such a good idea?

Dr. TERRY. That is right, sir.

Mr. LAIRD. So you think it is probably all right then for the Congress to continue with the practice of earmarking funds in the manner we have in the past?

Dr. TERRY. I do not think I am in a position to tell the Congress what they should do, sir.

Mr. LAIRD. I think your suggestion, though, is generally——

Dr. TERRY. I think it has been a very definite limitation in certain areas, and I think on other occasions it has been a stimulation.

Mr. LAIRD. Give me a few examples where you think earmarking in 1962 might be a stimulation?

Dr. TERRY. I am not sure that I can point out any.

Mr. FOGARTY. It would be easier to go back and give examples.

Mr. LAIRD. It usually would be easier to go back, but the problem that we are working on is the budget for next year. I personally have faith in the Public Health Service and in you as Surgeon General to run this program.

Dr. TERRY. Thank you, sir.

Mr. LAIRD. I think you can do a better job than I can as a Member of Congress, or than other Members of Congress or the Senate can do when it comes to setting priorities within these programs. I am surprised that you are reluctant to take the full responsibility for it.

Dr. TERRY. I am not reluctant to take the full responsibility. I would be very happy for the Congress to give us a lump sum. At the same time, I realize that one of the very stimulating factors in stimulating Congress to appropriate funds has been because of the interest in specific areas and specific programs. I would not like to lose that support and that interest that the Congress has. On the other hand, I am perfectly willing to take the responsibility for one lump sum given to the Service and to work with it.

Mr. Kelly. The reason why I wondered whether or not you could ask the Surgeon General to comment on 1961 instead of 1962 is, I cannot think of an instance where Congress earmarked funds from those that were requested. They essentially accepted the plans to carry out the expenditure of the funds that were requested and have earmarked the funds which they have added over and above the request. I think this is what the problem was as to why the Surgeon General could not answer.

Mr. Laird. Our committee has not done very much earmarking.

Dr. Terry. That is right.

Mr. Laird. We have not gotten into that area as much as the Senate has in the past, but it seems to me that when we get into the conference the earmarked items seem to do much better than your regular programs, and that always bothers me just a little bit. We seem to get the earmarked programs taken care of first, and what is left over goes into your regular program. That has been of concern to me, because I'm not sure that that leads to the most efficient use of the total funds.

I had hoped that some day we would be in a position where the Congress would follow the recommendations of the Public Health Service a little more closely, because I think you should have the professional ability and know-how in this field. When I speak of "you" I am talking about the Public Health Service.

Dr. Terry. Yes, sir. I understand.

Mr. Laird. We are getting to a position where the National Institutes of Health are really the responsibility of the Congress and not the responsibility of the Public Health Service. Do you understand what I am talking about?

Dr. Terry. I certainly do, sir.

Mr. Laird. The National Institutes of Health could be compared to the General Accounting Office and the Library of Congress. It is becoming an arm of the Congress rather than a part of the Public Health Service.

Dr. Terry. In terms of the size of our appropriation, that has certainly been true, sir.

Mr. Laird. Do you think that there is ever going to be a time in the future when we can look to the National Institutes of Health program as being truly a part of the Public Health Service in the sense that the other bureaus are? I thought the question that the chairman asked was a very good question, about the National Institutes of Health being separated from the Public Health Service. He was asking you whether it would be done in the future. I think it has already been done. Do you think that there is anything to that?

Dr. Terry. I think in terms of the responsibility for determining the size of our budget, that this is certainly true, Mr. Laird. It has been true over the past few years. No one more than I would like the opportunity to have that responsibility where it should exist, namely, in the hands of the responsible people in the Public Health Service and in the National Institutes of Health.

NIH BUDGET FOR 1962

Mr. Laird. You are a new Surgeon General and you made a very careful study of the budget of the National Institutes of Health. You had long experience in the National Institutes of Health, and served as the Acting Director of the Heart Institute. You prepared a budget which you submitted to the Secretary of Health, Education, and Welfare?

Dr. **Terry.** Yes, sir.

Mr. **Laird.** That provided for an increase in the NIH budget of $101 million.

Dr. **Terry.** Yes, sir.

Mr. **Laird.** That was your best judgment?

Dr. **Terry.** Yes, sir.

Mr. **Laird.** As to what the National Institutes of Health could use to carry on an effective program for 1962?

Dr. **Terry.** That is correct, sir.

Mr. **Laird.** Do you think that we would be getting to the point where you would have better control over this program if we followed your recommendation this year?

Dr. **Terry.** I do not know, sir.

Mr. **Laird.** You did not have any guidelines given to you by President Kennedy, or the Bureau of the Budget, or anyone else, in determining that particular figure?

Dr. **Terry.** We had guidelines, but not limitations, sir.

Mr. **Laird.** But there was no limitation imposed upon you, that you could not go above $101 million?

Dr. **Terry.** There was no suggestion that I could, should, or could not.

Mr. **Laird.** And you had complete freedom in the area of funding when you came up with that recommendation?

Dr. **Terry.** I had complete freedom in terms of making what I felt was the best recommendation that could be made for the National Institutes of Health.

LIVE POLIO VACCINE

Mr. **Laird.** I followed with interest your remarks about Dr. Sabin. Did you read that article in last night's paper, which was released, I think, out in Cincinnati?

Dr. **Terry.** Relative to the cost of the vaccine?

Mr. **Laird.** Yes.

Dr. **Terry.** I don't think I read last night's, but I know I read this morning's release.

Mr. **Laird.** Where does he get his figures that 30 million doses, I think he said, could be purchased for the amount of money that was asked of the Appropriations Committee?

Dr. **Terry.** I really do not know where he gets them and I do not think that he has any better basis than we do. They are both educated guesses and it is a question of which one is the best educated. I do not know.

Mr. **Laird.** That is all I have.

Mr. **Fogarty.** Mr. Michel.

RESEARCH ON PLUMBING FACILITIES

Mr. **Michel.** Dr. Terry, the other day I was contacted by a representative of the Associated Plumbing Contractors asking me to support an appropriation of a quarter of a million dollars for research on plumbing facilities. Does this come under the category of environmental health?

Dr. **Terry**. I do not know.

Mr. **Michel**. It is not, of course, a budgeted item.

Dr. **Terry**. May Dr. Anderson answer this, as he is in environmental health?

Mr. **Michel**. Yes.

Dr. **Anderson**. I have not heard about this, Mr. Michel, but we are engaged in the development of a better housing code, and part of the housing code activity usually relates to the plumbing code.

Mr. **Michel**. He referred to a study in Kentucky also. Have you folks had anything to do with that study?

Dr. **Anderson**. I do not know. I will try to get what information I can and be prepared to answer when I come back on environmental health.

Mr. **Michel**. It was all news to me and I said I would mention it when the time came here.

Dr. **Anderson**. Did he leave you with any kind of paper, Mr. Michel?

Mr. **Michel**. Yes, he did, but I forgot to bring it over.

Mr. **Fogarty**. I think we spent some money a few years ago on the development of standards for fixtures, didn't we? We had something to do with this. It has been before the committee a few times.

Mr. **Michel**. But my pointed question to you then would be, would this fall in the category of a proper area for you to research it in environmental health?

Dr. **Anderson**. It might. Without knowing what the specific proposal is that they had, I would say that it might. I would like to see it.

Mr. **Michel**. It would sound like something you might be interested in?

Dr. **Anderson**. I would like to see it.

CRITERIA FOR ADMISSION TO NIH

Mr. **Michel**. Doctor, you do have patients at the National Institutes of Health?

Dr. **Terry**. Yes, sir.

Mr. **Michel**. How many?

Dr. **Shannon**. 400—about.

Dr. **Terry**. About 400.

Mr. **Michel**. And what are the principal diseases or sicknesses that are treated?

Dr. **Terry**. Each of the seven Institutes, the categorical Institutes, have bed space and conduct outpatient studies of patients in the Clinical Center. The type of patients depends on the particular things that are being studied by that Institute at that time. For instance, the Heart Institute has approximately 100 beds. The Cancer Institute has about 125 beds. It goes down to the Dental Institute, which just has a few beds—five beds. Obviously, as you can understand, most of the dental studies can be done on outpatients.

Most of our studies in Heart cannot be done on outpatients, so we have both a large inpatient and outpatient volume. Usually our outpatients that take part, for example, are patients who have been referred to us by physicians and we are seeing these patients in order to get further information about these patients to see if they fit into our program. Or, for instance, if it is a child with congenital heart disease, we want to get a determination from our standpoint of how urgent the need to study and necessity to operate on this patient is.

Then another large aspect of our approach with relation to patients is followup studies. It is very important in many of our studies not only that we make the intensive studies which we do while the patient is in the hospital, but we have the opportunity without assuming full medical care responsibility for that patient, because we like to return them and want to return them to their physician if possible, but to have the opoprtunity to see them at appropriate intervals afterward as a followup type of check on the studies we have made in the hospital. And sometimes they will be mixed, with the patient being in the hospital and following that as an outpatient for a while, and then back in the hospital, and then as an outpatient, and back in the hospital, depending on the particular individual need for the study of the patient.

Mr. Michel. In part you answered my next question, which is going to be, What are the criteria for entering the hospital?

Dr. Terry. The criteria for entering the hospital are, first, that the patient must be referred by a physician, or a recognized referral agency, and by that I mean, for instance, as an example, we have a certain number of volunteers, normal volunteers, who come in and are referred through a church organization—a religious organization—but generally speaking, when we are speaking of patients they have to be referred by their physicians. Then they must have a disease which we are set up to study at the time, and sometimes it even amounts to having a particular stage of a disease, because often, for instance, we would be studying in the Heart Institute patients with high blood pressure and we would be using new experimental drugs on these patients. Obviously we would not want to use those drugs on many patients with advanced disease who had had a stroke or that were already in the late stages and a kidney deficiency, or congestive heart failure. So it amounts to the fact that the patient has to be referred by his physician first and, second, he must have a disease, and also a stage of the disease we are studying, or are set up to study at the time.

Mr. Michel. Do these patients mostly come from this area, or from all sections of the country?

Dr. Terry. A very large percentage of them come from this area. I think it is approximately 50 percent that come from within a 50-mile radius of the center of Washington, which would include Baltimore and go down toward Richmond and that area. The rest literally come from all over the country, and some from other countries.

Mr. Michel. That is all.

FRESH WATER SUPPLY BENEATH THE CONTINENTAL SHELF

Mr. Fogarty. I met some constituents this morning and they have done a lot of work on this idea which is that they could develop offshore fresh water supplies by going down underneath the Continental Shelf. They gave me this brief, which deals with the subject. I would appreciate it if you would take it and be prepared to discuss it with me before we conclude our hearings.

Mr. Fogarty. Thank you very much, Doctor. I think you did very well even though you have been in office for only a short time.

Dr. Terry. Thank you, sir and, I hope I can have more information the next time I appear before you.

NIH Budgets

Mr. Fogarty. We have asked for several things which will be placed in the record. In addition will you supply a statement on how the National Institutes of Health would spend another $100 million?

Dr. Terry. You mean another $100 million above the budget submitted to you?

Mr. Fogarty. Yes. Also for $60 million above and when we get to the detailed hearings on NIH we will expect Dr. Shannon to have professional judgment budgets like we asked for last year from each Institute as well as a complete history of the budget requests actually submitted.

Dr. Terry. Yes.

Mr. Fogarty. Thank you, Doctor.

(The budgets requested follow:)

Use by the National Institutes of Health of an additional $60,000,000 and $100,000,000 over the 1962 revised estimates

[In thousands]

	1962 revised estimate (1)	Additional $60,000,000 (2)	Total, cols. (1) and (2) (3)	Additional $100,000,000 (4)	Plan No. 4 total, cols. (1) and (4) (5)
Grants:					
Research:					
Regular programs:					
Continuations and supplements	$208,084	+$13,095	$221,179	+$13,095	$221,179
New:					
Carryover	15,353	−9,364	5,989	−9,364	5,989
"Wholly" new	50,025	+23,729	73,754	+35,834	85,859
Institutional research grants	14,500	+1,400	15,900	+2,500	17,000
Increase in overhead	2,000		2,000		2,000
Subtotal, regular programs	289,962	+28,860	318,822	+42,065	332,027
Special programs:					
Science evaluation grants	1,253		1,253		1,253
International medical research	5,000	+800	5,800	+2,500	7,500
Gorgas Memorial Laboratory	250		250		250
Clinical research centers	30,000	+21,500	51,500	+25,000	55,000
Primate centers	7,000		7,000	+5,000	12,000
Special resource centers		+5,000	5,000	+9,500	9,500
Subtotal, special programs	43,503	+27,300	70,803	+42,000	85,503
Total, research	333,465	+56,160	389,625	+84,065	417,530
Fellowships	22,000	+2,000	24,000	+2,000	24,000
Training	96,242		96,242	+4,000	100,242
State control programs	13,000		13,000		13,000
Community demonstration projects	2,000		2,000	+1,000	3,000
Total, grants	466,707	+58,160	524,867	+91,065	557,772
Direct operations:					
Research	64,112		64,112	+1,300	65,412
Biologics standards	3,050		3,050		3,050
Review and approval	9,846	+1,152	10,998	+1,964	11,810
Training activities	336		336		336
Professional and technical assistance	13,234	+388	13,622	+5,055	18,289
Chemotherapy contracts	22,538	+300	22,838	+300	22,838
Administration	3,177		3,177	+316	3,493
Total, direct operations	116,293	+1,840	118,133	+8,935	125,228
Total	583,000	+60,000	643,000	+100,000	683,000

NOTE.—The additional material for the record, referred to above, follows:

National expenditures for medical research by source of funds, 1958, 1959, 1960, 1961 [1]

[Millions of dollars]

Source of funds	Actual, 1958	Actual, 1959	Estimated, 1960 [2]	Estimated, 1961 [2]
Total	$490	$587	$715	$890
Government	239	307	400	526
Federal	226	290	377	496
State and local	13	17	23	30
Industry	170	190	215	250
Private support	81	90	100	114
Foundations and health agencies	45	49	55	62
Other private contributions	7	10	12	15
Endowment	19	19	19	19
Institutions' own funds	10	12	14	18

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[1] Coverage is limited to conduct and support of medical and health-related research. Support of other activities such as research training or capital outlays for research facilities are not included in this series.

[2] Data on Federal obligations are available at the beginning of the fiscal year; firm data on non-Federal expenditures cannot be obtained until after the end of the fiscal year. Therefore, the estimates for 1960 and 1961 may overstate the Federal share. These estimates are subject to revision pending completion of surveys of research expenditures by hospitals, State governments, medical schools, universities, and research institutes.

Source: Resources Analysis Section, Office of Program Planning, NIH, Feb. 7, 1961.

Federal expenditures for medical and health related research for fiscal years 1959, 1960, 1961

[Thousands of dollars]

Agency	1959 actual [1]	1960 estimated [1]	1961 estimated [1]
Total	$290,451	$377,390	$495,701
Atomic Energy Commission	16,091	17,802	19,800
Department of Defense	25,281	30,675	30,847
Department of Health, Education, and Welfare	236,033	312,904	424,972
(National Institutes of Health)	(211,705)	(284,989)	(385,300)
Veterans' Administration	11,033	13,415	16,665
Other	2,013	2,594	3,417
State Department (ICA)	501	731	711
Department of the Interior	19	20	21
National Science Foundation	1,329	1,448	1,700
Federal Aviation Agency	120	391	981
OCDM	40		
TVA	4	4	4

[1] Figures for 1959 are actual obligations. Figures for 1960 and 1961 are estimated obligations.

NOTES ON COVERAGE AND SOURCES

1. Coverage is limited to conduct and support of medical and health-related research. Support of other activities such as training or capital outlays for research facilities is not included in this series.

2. These data on Federal Government obligations for medical and health-related research are obtained by the National Institutes of Health directly from the agencies involved. The data cover: (*a*) All research supported by the constituent agencies of the Department of Health, Education, and Welfare (excluding the Office of Education); and (*b*) research expenditures in the medical sciences by the Department of Defense, Atomic Energy Commission, Veterans' Administration, and other agencies such as the Federal Aviation Agency, Office of Civil and Defense Mobilization, and the Department of State.

3. Coverage does not include research expenditures reported under biological sciences in Federal Funds for Science by the Department of Agriculture, the Atomic Energy Commission, or the National Aeronautics and Space Agency although some portion of the research supported by these agencies undoubtedly contributes to the fund of knowledge utilized by medical research. Similarly, these data do not include research expenditures of the National Science Foundation in the biological sciences which encompass a wide variety of fields such as botany, entomology, zoology, plant pathology, natural history, oceanography, ornithology, psychobiology, and experimental psychology.

Source: Resources Analysis Section, Office of Program Planning, NIH, Feb. 7, 1961.

Recent legislation affecting workload

Legislative item (descriptive title)	Public Law No.	Date effective	Workload impact
84th Cong.			
1st sess.			
To provide research and technical assistance relating to air pollution control.	159	July 14, 1955	Legislation extended by Public Law 86-365 approved Sept. 22, 1959. Workload impact reported under that act.
Mental Health Study Act of 1955	182	July 28, 1955	Authorized for a 3-year period, 1956-58, a grant-in-aid program of $1,250,000 for research into and study of resources, methods, and practices for diagnosing, treating, caring for, and rehabilitating the mentally ill.
Poliomyelitis Vaccination Assistance Act of 1955	377	Aug. 12, 1955	The grant program terminated June 30, 1957. The remaining activity on this program, consisting of the assembling and dissemination on vaccine production and shipment, continued until October 1960 and the processing of fiscal audit of State expenditures is expected to continue into fiscal year 1962.
2d sess.			
Dependents' Medical Care Act	569	Dec. 7, 1956	Added a new reimbursable beneficiary class—it is expected that in 1962 an average daily inpatient load of 158 dependents will be cared for, requiring 268 employees and a total cost of $1,950,000. These dependents are eligible for care on an outpatient basis without reimbursement—it is expected that in 1962 there will be 140,000 outpatient visits, requiring 115 employees and a total cost of $840,000. An average daily patient load of 150 dependents, including retired personnel are cared for in Federal uniformed service and non-Federal contract hospitals at an estimated cost in 1962 of $2,422,000.
National Health Survey Act	652	July 3, 1956	Authorized activities that will require, in 1962, 95 man-years and $2,468,100. The functions, personnel, and funds for this activity transferred to and included in the budget for the National Center for Health Statistics.
Federal Water Pollution Control Act	660	July 9, 1956	As of 1961, activity has increased by over $9,000,000, including $3,000,000 grants to States and interstate agencies. The major elements of the program which have been affected by the passage of the act are as follows:

BASIC DATA

National water quality network sampling for year ending Sept. 30, 1960

	Purpose of sample				Totals
	Chemical quality	Plankton population	Organic chemicals	Radiological activity	
Samples taken	2, 600	1, 100	500	2, 000	6, 200
Determinations made	44, 200	20, 900	7, 500	8, 150	80, 750

Water quality sampling stations as of Dec. 31, 1960	76
Sampling stations required	300

The basic data program was a new authorization to the Surgeon General to develop and make available data to enable water supply and pollution authorities, and others concerned to understand more adequately the scope and character of the problems they face, and more wisely to carry out their responsibilities. A water quality sampling network initiated in 1957 now has 76 of a planned 300 stations supplying regular samples for laboratory analysis by PHS, and cooperating laboratories.

CONSTRUCTION GRANTS

Workload data—Construction grants administration

	1957	1958	1959	1960	1961 [1]
Number of—					
Construction starts	145	511	501	556	563
Plants completed	4	145	446	436	550
Grants offers	446	592	545	573	570
Plans reviewed	216	526	558	565	570
Payment inspections	30	510	1,200	[1] 1,400	1,500

[1] Estimated.

Construction grants, providing Federal aid for the construction of waste treatment plants, is a new program responsibility authorized under Public Law 660. It is estimated that total grant expenditures under this program will be $135,052,000 by the end of fiscal year 1961.

ENFORCEMENT

Public Law 660 (84th Cong.) provides for Federal action to enforce the abatement of interstate pollution. Approximately 2,000 interstate water areas have been identified, each of which is to be studied and made the subject of a report. When 150 such areas were initially singled out for study, the results showed that between ⅔ and ¾ of these areas were seriously polluted. The program has held 12 formal conferences with respect to interstate pollution. 4 hearings so far have resulted from the failure of polluters to comply with recommendations of prior conferences. The 1st court action to be filed under the enforcement procedure, against St. Joseph, Mo., is now pending before a U.S. district court. The PHS has been requested to furnish expert witnesses, evidentiary materials, and exhibits. Revelations as to the radioactive contamination of the Animas River stimulated a demand for investigation and correction of pollution throughout the Colorado River Basin. The 1st session of the conference requested by 7 States was held in January 1960. The conference covered the Colorado River and its 60 tributaries and involves $\frac{1}{12}$ of the land area of the continental United States. An investigation, including radioactive pollution, has been instituted which will require some 5 years to complete. Other conferences will take place as the project develops.

Recent legislation affecting workload—Continued

Legislative item (descriptive title)	Public Law No.	Date effective	Workload impact
84th Cong.—Continued			RESEARCH
2d sess.—Continued			*Water supply and pollution control research projects*
			Enactment of Public Law 660 provided a broadened research program over prior authorization, to include investigations, experiments, and demonstrations. Research in water supply and pollution control is conducted at the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio. Current projects concern waste characterization, waste treatment, waste disposal, waste detection, and treatment of water.
			Technical services and comprehensive programs
			The technical services and related activities carried out under Public Law 660 provided to regional installations, States, and communities are concerned with (1) consultant services on problems such as methods for waste treatment, (2) the conduct of field investigations on problems such as the effect of pesticides on water quality, (3) the conduct of experiments and demonstrations, and the provision of assistance on scientific, engineering, economic, and administrative problems, and (4) administration of annual Federal grants of $3,000,000 to State and interstate water pollution control agencies to improve and extend their programs. Comprehensive programs are founded on basinwide studies of water requirements for all purposes and studies of pollution control problems, including those that will result from the anticipated uses of water. Major studies are now underway on the Great Lakes-Illinois River Basin, the Columbia River Basin, the Chesapeake Bay, and the Arkansas-Red Rivers.
Alaska Mental Health Enabling Act	830	July 28, 1956 [1]	A 9-member team of specialists conducted a comprehensive survey of construction needs in Alaska in 1956. Frequent consultative visits have been made in connection with the program. 9 payments ($2,000,000) were made to Alaska as program grants. Effective July 1, 1959, the administration of this grant was assumed by the Office of the President. PHS administers the $6,500,000 construction grant program; 11 payments have been made to date totaling $1,857,791.
Health Research Facilities Act of 1956	835	July 30, 1956	Authorized construction grant program of $30,000,000 annually. Administration requires about 23 man-years and $200,000 annually.
Health Amendments Act of 1956	911	July 1, 1956	Special project grants are provided to assist in the development of improved methods of care and treatment in the field of mental health; $14,300,000 has been appropriated for this purpose through 1961. Public Law 86-105 extended certain traineeship provisions of this act and workload data are shown there.
National Library of Medicine Act	941	Oct. 1, 1956	In 1961 this institution will operate with an appropriation of $1,738,000, involving 214 man-years. It will acquire 88,500 medical publications, catalog 23,500 titles, bind and repair 22,000 volumes, answer 10,000 inquiries, fill 120,000 loan requests, photograph 2,600,000 pages, and index 136,000 journal articles.
85th Cong.			
1st sess.			
3d Supplemental Appropriation Act, 1957 (amends sec. 364, pt. G, title III, of the Public Health Service Act).	85-58	July 21, 1957	Required substantial amount of staff time in establishing overtime payment policy and preparing related instructions and forms. Entails substantial amount of work in arranging with carriers for overtime services, and additional work in processing bills; a total of 14,714 overtime inspections were made in fiscal year 1959.

To authorize funds available for construction of Indian health facilities to be used to assist in the construction of community hospitals which will serve Indians and non-Indians.	85-151	Aug. 16, 1957	Projects have been approved with 12 community hospitals under this program providing for 88 beds for Indian use costing $1,784,000.
To amend the Immigration and Nationality Act, and for other purposes (amended by Public Law 86-253).	85-316	Sept. 11, 1957	Required substantial amount of staff time in collaborating with Immigration and Naturalization Service on preparation of regulations, instructions, and forms. Under sec. 15 of Public Law 85-316 over 21,000 physical and mental examinations have been given to refugees by PHS medical personnel (8,967 in 1958, 10,364 in 1959, and 1,827 in 1960). It is estimated that 500 examinations will be given in 1961. Under sec. 6 of Public Law 85-316 and Public Law 86-253 which amended that section, nearly 3,000 refugees afflicted with tuberculosis have been admitted through 1960 and 271 in 1961 through October.
2d sess.			
To amend the Agricultural Trade Development and Assistance Act of 1954 (Public Law 480).	85-477	June 30, 1958	Authorized the use of certain U.S.-owned foreign currencies for medical research projects in foreign countries. $3,707,000 was appropriated in 1961 and the estimate for 1962 is $10,084,000.
To amend sec. 314 (c) of the Public Health Service Act so as to authorize the Surgeon General to make certain grants-in-aid for provision in public or nonprofit accredited schools of public health of training and services in the fields of public health and in the administration of State and local public health programs.	85-544	July 22, 1958	Sec. 2 of the act which limits the period of authorization has been repealed by Public Law 86-720 which makes the legislation permanent. 12 schools will receive grants totaling $1,000,000 in 1962.
For the relief of certain distressed aliens (nationals of Netherlands in Indonesia and of Portugal in the Azores).	85-892	Sept. 2, 1958, to June 30, 1960.	Under this legislation 7,964 medical examinations were given in 1960.
86th Cong.			
1st sess.			
To extend certain traineeship provisions of the Health Amendments Act of 1956.	86-105	July 23, 1959	About 4,000 nurse traineeships—2,000 long term and 2,000 short term ($6,525,000)—and 625 public health traineeships ($2,000,000) will be awarded this year.
To amend the act of Aug. 5, 1954 (68 Stat. 674), and for other purposes.	86-121	July 31, 1959	Authorizes the provision of Indian sanitation facilities. Involves a cooperative program with the Indians. On the basis of a fully developed activity it is estimated that 95 man-years annually (primarily sanitary engineering and supporting sanitation staff) will be required.
To authorize construction of a toll bridge across the Rio Grande near Los Indios, Tex.	86-338	Sept. 21, 1959	The construction of these bridges would mean a shifting of traffic across the border. Even though the total workload might not be significantly increased, the volume of traffic over these 2 bridges would require additional staffing of 2 or more inspectors.
To authorize construction of a toll bridge across the Rio Grande near Rio Grande City, Tex.	86-343	do	
To provide for entry of certain relatives of U.S. citizens and lawfully resident aliens.	86-363	Sept. 22, 1959	Under this legislation 1,075 physical and mental examinations were given in 1960. As reporting of this category will not be separately identified for 1961 and thereafter, no estimate has been made for 1961.
Amendment to Federal air pollution control law	86-365	do	Legislation extended the Air Pollution Control Act through June 30, 1964, and authorized the program to make surveys and studies in addition to research and technical assistance. The program supports over 300 research projects involving program resources and other Federal and non-Federal organizations. Approximately 98 projects are supported through research grants. The National Air Sampling Network plans to expand from its present utilization of 172 local health and other air pollution control agencies to 185 in fiscal year 1961. Over 2,500 persons have participated in training courses provided by the Sanitary Engineering Center. In 1961, the plan is to support air pollution control curriculums in 10 universities and award 6 traineeships to qualified applicants.

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[1] Grants for mental health program effective July 1, 1957.

Recent legislation affecting workload—Continued

Legislative item (descriptive title)	Public Law No.	Date effective	Workload impact
86th Cong—Continued			RESEARCH—continued
1st sess—Continued			*Technical services and comprehensive programs*—Continued
Amendment to Atomic Energy Act of 1954	86-373	Sept. 23, 1959	PHS has assigned to the Federal Radiation Council 1 director-grade officer and 1 secretary. The estimated total PHS cost in 1961 is $117,000.
2d sess.			
To authorize and direct the Surgeon General of the PHS to make a study and report to Congress, from the standpoint of the public health, of the discharge of substances into the atmosphere from the exhausts of motor vehicles.	86-493	June 8, 1960	The Congress provided an additional $1,000,000 in 1961 to implement an accelerated research program on auto exhausts. The program, to comply with the mandate of Congress, has expanded its auto research facilities at the sanitary engineering center. Negotiations are currently underway, through the General Services Administration, to lease additional laboratory facilities at Cincinnati. Negotiations are also being carried on with the University of California to conduct auto exhaust studies, and arrangements are currently being completed for a small field station in Los Angeles County to study the problem there.
To establish a National Institute for International Health and Medical Research to provide for international cooperation in health research, research training, and research planning.	86-610	July 12, 1960	Reaffirms and specifies the present implied authorities of the Surgeon General for the support of health research and research training in foreign countries.
To enable the United States to participate in the resettlement of certain refugees.	86-648	June 14, 1960–July 1, 1962.	An estimated 8,000 medical examinations will be performed in the European area, 5,000 in 1961 and 3,000 in 1962.
To amend title III of the Public Health Service Act to authorize project grants for graduate training in public health and for other purposes.	86-720	Sept. 8, 1960	Considerable staff time required to develop forms, procedures, and a priority system. Eligible applicants oriented in the preparation of applications; applications reviewed by a board of experts in various professions involved and acted upon by the National Advisory Committee on Public Health Training. 58 grants made and administered. 136 applications have been processed from 135 of the schools that are eligible to receive funds. Grants totaling $2,000,000 will be awarded during 1962.
To amend title V of Agricultural Act of 1949, as amended, to extend period of admission on temporary basis of Mexican nationals for farm labor purposes.	86-783	July 1–Dec. 31, 1961.	This amendment continues until Dec. 31, 1961, the medical examination program which has been carried on since 1951 by the Division of Foreign Quarantine for the Department of Labor. During the period June 30 to Dec. 31, 1961, an estimated 358,000 medical examinations will be performed. This program is financed from farm labor supply revolving fund, Bureau of Employment Security, Department of Labor.
To amend the Public Health Service Act to authorize grants-in-aid to universities, hospitals, laboratories, and other public and nonprofit institutions to strengthen their programs of research and research training in sciences related to health.	86-798	Sept. 15, 1960	This program has not yet been implemented with 1961 funds. The law states that this program is to be financed with a transfer of not to exceed 15 percent of the funds for research projects.

REORGANIZATION OF THE PUBLIC HEALTH SERVICE

The Study Group on Mission and Organization of the Public Health Service, in its report published June 7, 1960, recommended reorganization of the Service. The report explores the present and probable future role of the Service during the next decade and sets forth the reasons reorganization is necessary in order to meet more effectively the future health needs of the American people.

The recommended organization includes an Office of the Surgeon General, a Bureau of Community Health, a Bureau of Environmental Health, a Bureau of Medical Services, and the National Institutes of Health. In addition, there would be the National Library of Medicine, a National Center for Health Statistics, and eight regional offices reporting directly to the Surgeon General.

The present bureau structure is defined in the Public Health Service Act and consequently no change in this structure is possible without legislative approval. Functional regrouping of divisions within the present bureaus, however, is desirable in any event, and does not have to await legislative reorganization of the bureau structure. To the extent considered desirable and practical, organizational moves toward the recommended structure, which could be made without specific legislative authority, have been or are being accomplished as explained below.

In consonance with the recommendations of the study group, the Surgeon General, with the approval of the Secretary, has made changes as follows:

Office of the Surgeon General.—The Division of Health Mobilization has been transferred from the Bureau of State Services to the Office of the Surgeon General. Also a National Center for Health Statistics has been established in the Office of the Surgeon General, pending enactment of legislation which will permit the Center to be set up as a separate component of the Service. The National Office of Vital Statistics (formerly a part of the Bureau of State Services) and the National Health Survey (previously part of the Division of Public Health Methods in the Office of the Surgeon General) have been transferred to the National Center for Health Statistics.

Bureau of Medical Services.—Three divisions, Dental Resources, Health and Medical Facilities, and Nursing Resources have been transferred from the Bureau of Medical Services to the Bureau of State Services as a part of the program for implementing the reorganization of the Service.

Bureau of State Services.—In keeping with the plans for dividing the existing Bureau of State Services into a new Bureau of Community Health and a new Bureau of Environmental Health steps have been taken to group separately within the Bureau of State Services those divisions primarily concerned with community health and those primarily concerned with environmental health.

Community health divisions.—In accordance with the above grouping, the Division of Dental Resources, which was transferred from the Bureau of Medical Services to the Bureau of State Services, has been combined with the Division of Dental Public Health to become the new Division of Dental Public Health and Resources. Similarly, the Division of Nursing Resources, which was transferred from the Bureau of Medical Services to the Bureau of State Services, has been combined with the Division of Public Health Nursing to become the new Division of Nursing. In addition, the Division of Hospital and Medical Facilities has been transferred from the Bureau of Medical Services to the Bureau of State Services. The Division of Special Health Services and the Division of General Health Services have been abolished and replaced by the Division of Accident Prevention, the Division of Chronic Diseases, and the Division of Community Health Practice. The above divisions, together with the Communicable Disease Center, now make up the group of community health divisions.

Environmental health divisions.—The remaining divisions of the Bureau of State Services fall into the category of environmental health. These include Air Pollution Control, Occupational Health, Radiological Health, Water Supply and Pollution Control, and the Division of Engineering Services.

In the near future the Division of Engineering Services will be abolished and replaced by the Division of Milk, Food, Interstate and Community Sanitation.

Legislative approval will be required to—

(*a*) Establish the National Center for Health Statistics as a separate organizational entity. It is now carried, temporarily, in the Office of the Surgeon General.

(*b*) Establish a Bureau of Community Health to be comprised of the "community health divisions" presently within the Bureau of State Services.

(*c*) Establish a Bureau of Environmental Health to be comprised of the "environmental health divisions" presently within the Bureau of State Services.

(*d*) Abolish the Bureau of State Services.

A bill has been drafted proposing greater flexibility, through administrative actions by the Surgeon General and the Secretary, in the establishment and modification of organization units of the Public Health Service.

AWARDS AND HONORS FROM NON-FEDERAL ORGANIZATIONS, CALENDAR YEAR 1960

NATIONAL INSTITUTES OF HEALTH

Name	*Award*
Andrews, Justin M., Director, National Institute of Allergy and Infectious Diseases.	The Joseph Augustin LePrince Award for outstanding accomplishments in the field of malaria. Presented by American Society of Tropical Medicine and Hygiene.
Birren, James E., National Institute of Mental Health.	First Annual Stratton Award of the American Psychopathological Association ($500 stipend).
Blum, Harold F., National Cancer Institute.	Sigma Xi Award.
Fitzgerald, R. J., and Keyes, P.H., National Institute of Dental Research.	Annual Research Award of the Chicago Dental Society.
Heppel, Leon A., National Institute of Arthritis and Metabolic Diseases.	The Hillebrand Award of the American Chemical Society, Washington, D.C.
Jacobs, Leon, National Institute of Allergy and Infectious Diseases.	(1) Fellowship, Fulbright; (2) Fellowship, Simon Guggenheim Foundation.
Rowe, Wallace P., National Institute of Allergy and Infectious Diseases.	Eli Lilly & Co. Award in bacteriology and immunology, a bronze medal and $1,000, from the Society of American Bacteriologists.
Thruman, Ernestine, Division of Research Grants.	Chosen Professional Woman of the Year by District of Columbia State Federation of Business and Professional Women's Clubs.
Wildman, William C., National Heart Institute.	Fellowship, Simon Guggenheim Foundation.

BUREAU OF STATE SERVICES

Black, Luther A., Sanitary Engineering Center.	Citation award for developing and improving laboratory procedures in sanitary milk control presented annually to member of International Association of Milk and Food Sanitarians who has contributed greatly to milk and food sanitation.
Febles, Francisco, Communicable Disease Center.	Citation from the Puerto Rican Women's Committee of Philadelphia in recognition of his contributions to humanity through medical research and service in community relations.
Goldman, Morris, Communicable Disease Center.	Received an award of honor from Brooklyn College, N.Y., as one of its distinguished alumni.
Hayes, W. J., Jr., Communicable Disease Center.	Certificate of honorary membership from the National Pest Control Association in recognition of his guidance on toxicological problems related to pesticides.
Hope, Malcolm C., Division of Engineering Services	Commendatory certificate from the National Association of Plumbing Contractors in recognition of his services to the industry.

Name	*Award*
Law, Frank E., Division of Dental Public Health and Resources	Certificate from the Maryland State Dental Association for valuable services rendered in elevating the standards and advancing the science of dentistry.
Light, Israel, Division of Engineering Services	Special certificate from the National Science Teachers Association in recognition of his having established the science teacher achievement recognition program, a program designed to develop better public school science instruction.
Miller, John H., Division of Special Health Services	A medal from the American Heart Association and a certificate from the Board of Directors of the New Hampshire Heart Association for his distinguished service and leadership in advancing the heart program in New Hampshire.
Neill, Arthur H., Division of Engineering Services	Certificate of meritorious achievement from the Commonwealth of Puerto Rico for his zealous and outstanding contribution to the successful eradication to malaria in the island.
Pelton, Walter J., Division of Dental Public Health and Resources	A plaque from the Human Factors Research Division, School of Dentistry, University of Southern California, in appreciation and acknowledgement of his outstanding contributions to the program.
Pratt, Harry, Communicable Disease Center	Certificate of recognition from the Puerto Rico Department of Health for his outstanding work in malaria control.
Ryder, Claire, Division of Special Health Services	Elected president of the American Medical Women's Association.
Shortal, Hazel, PHS nursing consultant, region IX	University of St. Louis Merit Award at Founders Day Celebration as the graduate who personifies the highest ideals of St. Louis University.
Stout, Genevieve, Communicable Disease Center.	Resolution of commendation from the Association of State and Territorial Public Health Laboratory Directors for her services rendered in field consultation work.
Tompkins, Paul C., and Van Sandt, Max, Division of Radiological Health.	Pfizer Merit Awards from the Charles Pfizer & Co., Inc., at the U.S. Civil Defense Council for their work in promoting civil defense program in America.
Whitney, John M., Division of General Health Services, Region VII.	Pfizer Merit Award at the U.S. Civil Defense Council from the Charles Pfizer & Co., Inc., for his "endeavor in the interest of civil defense, disaster medical care, radiological, biological, and chemical nonmilitary defense and mass casualty care".
Woodward, Richard L. and Walton, Graham, Sanitary Engineering Center.	Honorable mention for scientific paper in the Resources Division Competition of the American Water Works Association.

Name	*Award*
Milk and Food Program, Division of Engineering Services.	Plaque from the National Restaurant Association for its accomplishments in the field of food sanitation.
Hosey, Andrew D., and Mendenhall, Alfred L., Jr., Occupational Health Field Headquarters.	Award by the Michigan Industrial Hygiene Association for outstanding work in industrial hygiene, particularly for the development and use of the Envirec, an instrument for continuous recordings of environmental air, wet-bulb, globe temperatures, and air velocity—four factors generally used for evaluating exposure to a hot environment.
Irving, Laurence, Arctic Health Research Center.	Elected to honorary membership in the Canadian Physiological Society.
Brown, W. J., Simpson, W. G., and Deacon, Wilbur E., Venereal Disease Center.	Award from the American Medical Association for the exhibit on fluorescent antibody technique in venereal disease diagnosis.
General Engineering Program	The Metropolitan Planning Exhibit Award for the exhibit "Guiding Environmental Development for Better Community Health," at the American Public Health Association meeting.

BUREAU OF MEDICAL SERVICES

Archambault, George F., Chief, Pharmacy Branch, Division of Hospitals.	(1) Honorary Ph. D. (doctor of pharmacy) degree, Massachusetts College of Pharmacy; (2) Elected to membership, Board of Trustees of U.S. Pharmacopoeia (1960–70); (3) Elected to chairmanship, Council of the American Pharmaceutical Association.
Hiebert, Daniel H., Medical Officer in Charge, U.S. Public Health Service Outpatient Clinic, Provincetown, Mass.	Named "General Practitioner of the Year" by the Barnstable County Medical Society and by the Massachusetts Medical Society.
MacKillop, Mew. Nagle, Clifford B. Reynolds, Robert N. U.S. Public Health Service Hospital, Fort Worth, Tex.	Certificates "for outstanding service" awarded by the Fort Worth Federal Business Association.
Perkins, Ralph L., Administrative Officer, U.S. Public Health Service Hospital, Staten Island, N.Y.	Cited by Hospital Management magazine for writing the best article on hospital public relations in 1960.
Van Son, Marie H., Assistant Director of Nursing for Training, U.S. Public Health Service Hospital, Fort Worth, Tex.	Received the 1960 "Civil Servant of the Year" award of the Fort Worth Federal Business Association.

OFFICE OF THE SURGEON GENERAL

Burney, Leroy E., Surgeon General	Honorary degree of doctor of science, Women's Medical College of Pennsylvania.
Knutson, John W., Chief Dental Officer	(1) Award of Merit from Georgetown University for Contributions to the Dental Profession, (2) Honorary degree of doctor of science, University of Pennsylvania.

Name	*Award*
Leone, Lucile Petry, Chief Nurse Officer.	Citation from University of Buffalo for distinguished leadership in the field of nursing and public health.
Porterfield, John D., Deputy Surgeon General.	Honorary membership in Delta Omega.
Smith, Robert L., Medical Director. Deputy Chief, Division of Health Mobilization.	Pfizer Merit Award at the U.S. Civil Defense Council for meritorious service in civil defense and disaster medical care, sponsored by Charles Pfizer & Co., Inc.
NATIONAL LIBRARY OF MEDICINE	
MacDonald, M. Ruth, Office of the Director.	The Margaret Mann Citation for 1960 given by the American Library Association for "distinguished and devoted service in the field of cataloging and classification, as well as for high ideals and outstanding leadership which have made a distinct advancement of the library profession as a whole."

Monday, March 20, 1961.

BUILDINGS AND FACILITIES

WITNESSES

HARRY L. DORAN, CHIEF FINANCE OFFICER

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. THEODORE J. BAUER, CHIEF, BUREAU OF STATE SERVICES

DR. C. A. SMITH, MEDICAL OFFICER IN CHARGE, COMMUNICABLE DISEASE CENTER

DR. LUTHER L. TERRY, SURGEON GENERAL

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
PUBLIC HEALTH SERVICE			
25 Other services	213	208	75
26 Supplies and materials	46		
31 Equipment	732	59	
32 Lands and structures	145	932	474
Total, Public Health Service	1,136	1,200	549
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
21 Travel and transportation of persons		3	3
24 Printing and reproduction	17	13	17
25 Other services	315	2,022	9,693
31 Equipment	226	312	762
32 Lands and structures	8,119	3,076	3,241
Total, General Services Administration	8,677	5,426	13,716
Total obligations	9,814	6,625	14,264

Program and financing

[In thousands of dollars]

	Costs to this appropriation					Analysis of 1962 financing			
	Total estimate	To June 30, 1959	1960 actual	1961 estimate	1962 estimate	Deduct selected resources and unobligated balance, start of year	Add selected resources and unobligated balance, end of year	Appropriation required for 1962	Appropriation required to complete
Program by activities:									
1. Communicable disease center	12,600			400	4,200	200	8,000	12,000	
2. Construction of animal quarters (at the National Institutes of Health, Bethesda, Md.)	2,606	1,217		94	489	1,210	806	85	
3. Research facilities construction and site acquisition	11,000		147	239	1,329	14	1,485	2,800	7,800
4. Construction of General Office Building No. 2 (NIH)	700				448		252	700	
5. Middle America Research Unit housing	400				389		11	400	
6. Construction of master utilities extension (NIH)	645				459		186	645	
7. Environmental health center	785			450	335	306			
8. Construction of research facilities, Lexington, Ky	350			21	311	329	18		
9. Extension of Clinical Center cafeteria	335			29	306				
10. Construction of animal quarters, Hamilton, Mont	150		147	3					
11. Construction of library facilities	7,300	283	1,947	3,544	907	1,527	620		
12. Construction of dental research building	3,799	303	1,800	1,695					
13. Construction of surgical facilities	1,965	98	976	891					
14. General office building	9,925	346	2,070	6,300	1,041	1,209	168		
15. Equipment, Communicable Disease Center	1,700	264	986	450					
16. Construction of biologics standards laboratory building	3,500	2,157	1,268	76					
17. Construction of research facilities (Clinical Center, NIH)	61,126	61,126							
Total program costs	118,886	65,794	9,340	14,191	10,214	4,795	11,546	16,630	7,800
18. Relation of costs to obligations:									
Costs financed from obligations of other years, net (−)				−7,566					
Obligations incurred for costs of other years, net			474		4,050				
Total obligations			9,814	6,625	14,264				
Financing:									
Unobligated balance brought forward			−14,295	−4,548	−1,699				
Recovery of prior year obligations			−74						
Unobligated balance carried forward			4,548	1,699	4,065				
Unobligated balance lapsing			307						
New obligational authority			300	3,776	16,630				
New obligational authority:									
Appropriation			300	3,470	16,630				
Reappropriation				306					

General Statement

Mr. Fogarty. The committee will come to order. Mr. Doran, do you have a statement?

Mr. Doran. I have a statement to file for the record, and a short summary which I will read, Mr. Chairman.

Mr. Fogarty. All right, go ahead.

(The statement follows:)

Statement by Chief Finance Officer, Public Health Service

Mr. Chairman and members of the committee, the appropriation, "Buildings and facilities, Public Health Service," was established by the 1961 Appropriation Act as a means of consolidating into one account a number of the construction projects of the Service. The 1962 budget estimate includes six programs, three of which represent continuations of projects for which funds were appropriated in the 1961 act. The total estimate for 1962 is in the amount of $16,630,000, and is to finance the following items:

COMMUNICABLE DISEASE CENTER ($12 MILLION)

Plans for the recently completed buildings at the Communicable Disease Center in Atlanta were developed in 1954. At that time, the space planned was adequate for programs then in existence and allowed for moderate expansion. During the intervening time until occupancy in July 1960, program increases, changes in laboratory technology, and organizational changes, including the transfer of the venereal disease program and the tuberculosis program to the Communicable Disease Center have made it impossible for the new facilities to house these expanded activities.

Some functions of the center are still located at Chamblee, Ga. These include the following: Venereal Disease Research Laboratory, Tuberculosis Research Laboratory, Toxicology Section, Southeastern Rabies Field Station, a leprosy research project, the entire animal breeding and holding program, warehousing for the center, maintenance shops, and scientific services. Studies made by the General Services Administration, representatives of the Bureau of the Budget, and CDC personnel, indicate that it would not be to the best interests of the Government to continue use of the Chamblee location. Activities located in areas other than Chamblee, which will be brought into the new facility when space becomes available, include the Biophysics Section (Savannah, Ga.) and the Venereal Disease Experimental Laboratory (Chapel Hill, N.C.).

To house these activities, additional laboratories, infected animal areas, offices, warehousing, and space for supportive scientific, and program services will be required at the new center.

In addition to the increased space needs on the Clifton Road site, certain supporting facilities must be provided at an offsite location. These include animal breeding, holding, and grazing facilities; animal processing laboratories; storage; certain program services; necessary programs requiring maximum security or large experimental animals; and quarters for animal caretakers.

The sum of $600,000 was provided in the 1961 appropriation to be used for the acquisition of land and the development of plans and specifications for the additional buildings required at the site of the new center and at the offsite location. The 1962 estimate would provide funds for construction of the facilities. Since plans for this construction program are in the developmental stage, decisions as to scope, size, and cost are not yet firm.

CONSTRUCTION AND EQUIPMENT, ANIMAL QUARTERS ($85,000)

This item would provide funds to convert space in the National Institutes of Health animal production facility (wings 14F and G) to provide for proper control, rigid caretaker practices, and testing procedures in the breeding of specific pathogen-free (SPF) animals. Funds were provided in the 1961 appropriation for the construction and equipment of cage-washing facilities, for the purchase of cages, and for other alterations to this building.

It has become evident that modern research methodology requires more and more use of this type of animal. Production methods for SPF animals differ from the conventional production methods in the following ways:

1. Parent stock for breeding colonies are all cesarean delivered and foster nursed on disease-free mothers—possibly originating from a germ-free environment.

2. All rations fed to SPF animals are prepared using methods which insure "pasteurization" temperatures throughout each particle of feed at some stage in the manufacturing process. All feed is "dispensed" by the feed manufacturer in hermetically sealed metal cans.

3. All air entering the colony is filtered. Appropriate air pressure gradients must be established between SPF rooms and adjacent areas.

4. All cages are autoclaved after being washed and just prior to being returned to colony rooms. Cages must not be interchanged between "SPF" and "conventional" colony rooms.

5. All inanimate objects (cages, feed cans, refuse cans, etc.) enter or leave each colony room via a steam lock.

6. Caretakers are required to completely change clothing and to observe other very strict regulations upon entering or leaving colony rooms through specialized personnel locks. Only the most skillful and dependable caretakers are selected for these positions.

7. A testing protocol must be established to determine the presence or absence to selected infections in the colonies and of any changes which occur in this regard.

8. Concomitant with the installation of SPF facilities in the production area must be the development of similar facilities in the laboratory areas. Otherwise, animals issued and held in "conventional" quarters would very quickly acquire "conventional" infections and the advantages of SPF production would be quickly voided—except possibly for animals used in very short-term experimental procedures.

RESEARCH FACILITIES CONSTRUCTION AND SITE ACQUISITION ($2,800,000)

Funds were provided in the 1960 and 1961 appropriations for the initial expenses of acquiring and developing a farm to be used by the National Institutes of Health for animal research and production. This budget estimate provides for part of the construction costs, and for additional planning and design.

Title to a farm was acquired by the Federal Government in May 1960. The farm will be operated by the Division of Research Services which serves as a source of supply of animals used by the several Institutes and Divisions in research and also for the long-term holding of animals under observation for research purposes. Added facilities on Government-owned property outside of Bethesda were required for the following reasons: (*a*) continuing increase in the number and variety of animals and animal types needed for research; (*b*) an increasing proportion of animals under long-term holding (1 to 5 years); (*c*) insecurity of limited space used at Casey Farm, formerly the NIH farm; (*d*) overcrowding of laboratory aids branch animal facilities at NIH, Bethesda.

Further needs for space and facilities at the new farm which have developed more recently comprise:

(*e*) Developing need for increasing the length of the quarantine period for dogs from 2 to 4 weeks due to the deteriorating quality of these animals which are obtained from commercial sources, with proportionate increase in the laboratory aids branch dog popualtion.

(*f*) Termination of the contract with Casey Farm on July 1, 1960.

(*g*) Major increase in additional research facilities at the Bethesda reservation which will have the effect of accelerating the growth rate of animal populations needed for research.

The principal effect of these new developments on the planning of facilities needs and construction of the new farm has been to advance the schedules of animal population occupancy. This is especially applicable to dogs and cats. In a previous timetable, it was estimated that by 1965, a total of 500 dogs and 500 cats would be kept at the new farm. These two species, which use kennel facilities in common, amount to a dog population equivalent of 750 animals. It is now expected that this value will be reached by 1963. It is also anticipated that there will be some stepping up of requirements for farm-type animals. These animals are kept in shelters and stalls.

In a breakdown of costs which follows, provision has been made in the 1962 estimate for—

(1) Construction of utilities, perimeter fencing and tree planting, water supply, sewerage, incinerator, waste chemicals disposal, telephone, electric power and distribution, heating and air conditioning, roads, parking and loading space—all mainly staged construction	$935, 575
(2) Construction of 2 functional buildings:	
(*a*) A kennel building with service wing for dogs and cats. This building will have a population saturation value of 600 dog-equivalents in runs and a normal occupancy value of 460 dog-equivalents. There will also be cages in the sickbays for 250 dogs or 250 cats	930, 000
(*b*) A barn building with service wing. This building will provide shelter on an intermittent basis, and feed storage for the 335 farm-type animals formerly scheduled for 1965 and now advanced in time. The buildings will have facilities ancillary to research and for treatment in the service wings (such as for the initial processing of specimens, bleeding, isolation, surgery, autopsy, etc.)	249, 200
(3) Planning and design funds to complete design for 1962 construction and for 1963 construction	323, 425
(4) Contingencies for 1962 planning and construction	361, 800
Total	2, 800, 000

CONSTRUCTION OF GENERAL OFFICE BUILDING NO. 2 ($700,000)

The general office building now under construction for the National Institutes of Health will be available for occupancy in the first quarter of 1962. At the time this structure was being designed, the proposed size was planned to permit relocating on the Bethesda reservation all NIH staff then located in rented space. However, programs have continued to grow during this interval, and it is now estimated that it will be necessary to continue to house about 1,000 employees in rented space when the general office building is occupied.

The National Institutes of Health has utilized rented space over an extended period of approximately 5 years. The experience during that time demonstrates the impracticability of continuing this practice on a permanent basis. Even at premium prices, office facilities properly designed for NIH functions are not available in nearby areas. The use of substandard office space and makeshift arrangements in structures designed as apartment dwellings results in inefficiencies which are not only expensive, but also serve as a deterrent to effective operations. Separating programs from the parent organization and from each other creates many problems of communication and program direction and results in additional expenses for servicing. These are real costs in addition to the identifiable rental charge currently averaging $600,000 annually.

The circumstances dictate the need for planning and constructing a second office building on the Betheseda reservation. It is proposed, therefore, to begin planning in 1962 for a facility with space to house approximately 1,400 employees. A structure of this size will permit some space for adjustment as a result of possible future growth or for the relocation of office staff presently housed in areas which could be converted to research laboratories should the need arise. Total planning and construction time is estimated at 3 years. The $700.000 in planning funds requested in this budget would permit planning to be started early in 1962, with construction to begin about midyear in 1963. Construction costs for this facility are currently estimated to approximate $10 million.

MIDDLE AMERICA RESEARCH UNIT HOUSING ($400,000)

The lack of housing facilities available to NIH personnel stationed at the Middle America Research Unit in the Canal Zone has been a continuous problem since the establishment of the Unit. The only housing officially assigned to the Public Health Service by the Canal Zone Government consists of two substandard units rented from the Panama Canal Company and inconveniently located some 20 miles from the laboratory. Practically all officers and civilian employees must domicile in the Republic of Panama as there is no available rental housing in the Canal Zone. This has created a hardship on all of the staff of the Middle

America Research Unit. Those of the staff assigned quarters in the Canal Zone are inadequately and tenuously housed and must commute long distances, while those who live in the Republic must pay exorbitant rents.

At the present time living quarters are required for 12 staff members and their families. The Canal Zone Government has offered to make available at no cost, adequate building sites adjacent to a site now being prepared by the Federal Aviation Agency for housing units which are now under construction. An appropriation of $400,000 is requested to develop land, and plan and construct six duplex family quarters, consisting of six 2-bedroom units and six 3-bedroom units.

This cost estimate was developed through consultation by representatives of the National Institute of Allergy and Infectious Diseases with representatives of the Federal Aviation Agency at the Canal Zone. The cost for construction is expected to average about $22,250 per unit. Clearing of land, landscaping, roadways, sewers, and other utilities are estimated at $113,000, and planning specifications and supervision at $20,000.

CONSTRUCTION OF MASTER UTILITIES EXTENSION ($645,000)

The operating utility resources for the National Institutes of Health will reach their capacity with the completion of structures presently under construction at the Bethesda reservation. Extensive advancements to the central utility resources are now necessary to insure that there will be an adequate system available to service additional proposed structures.

With the completion of a master utility survey by Nottingham & Associates, management-engineering consultants, a detailed outline of requirements for the central utility resources has been developed to serve all additional structures presently plotted on the NIH master plot plan. Their recommendations indicated that there is an urgent need to (1) revise and expand our electrical system to provide additional capacity and flexibility, (2) make extensive alterations to the master fire alarm and watchman report system, and (3) construct a second steam line to the clinical center. It is estimated that $7,420,000 will be required for the planning and constructing of the total project.

A total of $645,000 is requested in 1962 for the design and planning of the entire system ($610,000) and for the construction of the steam line from the central main to the clinical center ($35,000). Due to the complexity and diversity of the engineering features involved and due to the continued expansion of the National Institutes of Health, funds are requested at this time for the development of engineering plans for the entire system. A piecemeal approach to this project over several years would result in a more complex and more costly system.

Approximately 1 year will be required to complete the planning and design for the additions to the utility system while it is estimated that the construction will cover a span of 2 years. The steam line construction is necessary in 1962 to provide as quickly as possible standby capacity in the event of a major breakdown in the primary service line.

The first project included in this appropriation item is for the use of the Bureau of State Services. The remaining five projects are for the National Institutes of Health. Both Dr. Shannon, Director of the National Institutes of Health, and Dr. Smith, medical officer in charge of the Communicable Disease Center, are here today and are available to answer any questions that you may have about their building programs.

1962 BUDGET

Mr. Doran. Mr. Chairman and members of the committee, this is the second year for a consolidated appropriation under which most direct construction items of the Public Health Service are financed. Only funds for construction of facilities for Indian health acitivities and for certain NIH facilities which were started under separate appropriations are excluded. The estimate of $16,630,000 for 1962 provides funds for the following projects:

Additional facilities for the Communicable Disease Center ($12 million);

Provision of space at the National Institutes of Health for the breeding of specific pathogen-free animals ($85,000);

Part of the construction costs, and further planning in connection with the National Institutes of Health animal farm ($2,800,000) ;

Planning for the construction of a second general office building at the National Institutes of Health ($700,000) ;

Housing for personnel assigned to the Middle America Research Unit ($400,000) ; and

Design and planning of a master utilities extension, and construction of a steam line, at the National Institutes of Health ($645,000).

The first project included in this appropriation item is for the use of the Bureau of State Services. The remaining five projects are for the National Institutes of Health. Both Dr. Shannon, Director of the National Institutes of Health, and Dr. Smith, Medical Officer in Charge of the Communicable Disease Center, are here today and are available to answer any questions that you may have about their building programs.

PROPOSED LANGUAGE OF PREAMBLE

Mr. FOGARTY. You have quite a few changes in the language, don't you—in the preamble?

Mr. DORAN. One is for an increase in the number of commissioned officers—from 2,100 to 2,600. Another change would increase the allowance for education of dependents of personnel stationed in foreign countries.

Mr. FOGARTY. Do you think you would have any problem getting 500 additional public health officers?

Mr. DORAN. These are officers for the regular corps. A large part of these will be filled by converting from reserve to regular; so there would be no problem as far as utilizing the number, Mr. Chairman.

The change with respect to purchase, erection, and maintenance of temporary or portable structures was put in the preamble paragraph rather than repeat it in several of the appropriations, where it has been provided for before. The last change relating to the increase in the number of positions that might be required under section 208(g) is deleted because that is now part of the permanent legislation and does not need to be repeated.

Mr. FOGARTY. Do you have much legislation that is subject to a point of order now in the bill?

Mr. DORAN. There are some items, Mr. Chairman, subject to a point of order. We have been working on legislation that would provide for these items in basic legislation.

COMPLETION OF CONSTRUCTION

Mr. FOGARTY. Are all of these requested amounts for the completion of the units? Will all these projects be completed in the next fiscal year?

Mr. DORAN. Not all of them, sir.

Mr. FOGARTY. Which ones won't?

Mr. DORAN. Starting on page 7, the Communicable Disease Center: The planning money was apportioned this year and we are asking for construction money in 1962. That would extend over at least until 1963 before it would be completed. The construction of the animal quarters at the National Institutes of Health——

Mr. FOGARTY. That is nearly completed?

Mr. DORAN. It is underway, but there is $85,000 additional requested for further expansion of that work in 1962. The third item, research facilities construction and site acquisition: That applies to the NIH animal farm. This will extend over a period of years. The construction of office building No. 2: We are asking for planning money.

The Middle America Research Unit is for housing in the Panama Canal Zone. We anticipate letting the contracts in fiscal year 1962, and the work would probably extend into the next year.

The construction of the master utilities extension: Most of this is planning money for the major project, and we will be in later for construction money. The Environment Health Center: $785,000 in 1961 is for the planning for the Environmental Health Center.

Construction of research facilities at Lexington, Ky.: Part of the planning will be done this year and the construction contracts awarded in 1962. The money was provided last year for the extension of the Clinical Center cafeteria. That has not been completed and is not underway as yet.

The construction of animal quarters in Hamilton, Mont., is pretty well completed, is it not, Dr. Shannon?

Dr. SHANNON. It was completed in June 1960.

Mr. DORAN. The construction of the library facilities: That was due to be completed in June. It is a little behind schedule, but the latest estimate is some time in the month of August 1961.

The dental building is practically finished. The surgical facilities will be finished within a few months. The general office building is well underway. Do you have the scheduled date of completion?

Dr. SHANNON. It will be open this summer—completely occupied this fall.

Mr. DORAN. The biologics standards laboratory building is occupied.

NEW PROJECTS, 1962

Mr. FOGARTY. Now you have six requests for new projects. Will you go down and explain each one of them.

COMMUNICABLE DISEASE CENTER

Mr. DORAN. The first one, the Communicable Disease Center: Dr. Smith is here.

Dr. SMITH. As you know, Mr. Fogarty, we are in new quarters which house——

Mr. FOGARTY. You are asking for $12 million now.

Dr. SMITH. Yes, sir. This will allow us to combine all of our activities in the Clifton Road Center and at the animal farm, which is going to be just a couple of miles from Lawrenceville—about 20 miles from the new center. This will allow us then to abandon Chamblee.

It also includes combining some of our activities at the Clifton Road Center that are now housed in other areas such as Washington, Chapel Hill, and Savannah.

Mr. FOGARTY. When will this be completed?

Dr. SMITH. According to our schedule, we would hope to move into it on September 1, 1963.

NIH ITEMS

Mr. FOGARTY. What is the next one—$85,000?

Dr. SHANNON. This pertains to "Construction and equipment, animal quarters," at Bethesda. This and the other items are all NIH. We have prepared descriptions of each of these items for submission, which, if you wish, we can put in the record and discuss.

Mr. FOGARTY. We will put them in the record.

CONSTRUCTION AND EQUIPMENT, ANIMAL QUARTERS

1962 appropriation estimate, $85,000

It has become evident that modern research methodology requires more and more use of specific pathogen-free (SPF) animals. In order to provide these animals which are necessary to the progress of many experimental studies it is essential to develop specialized quarters in the Bethesda animal production facility. Funds in the amount of $85,000 are requested in 1962 to convert space in wings 14 F and G to provide for proper control, rigid caretaker practices and testing procedures required in the breeding of these animals.

Production methods for pathogen-free animals differ from the conventional production methods in the following ways:

1. Parent stock for breeding colonies are all cesarean delivered and foster nursed on disease-free mothers—possibly originating from a germ-free environment.
2. All rations fed to SPF animals are prepared using methods which insure "pasteurization" temperatures throughout each particle of feed at some stage in the manufacturing process. All feed is "dispensed" by the feed manufacturer in hermetically sealed metal cans.
3. All air entering colony is filtered. Appropriate air pressure gradients must be established between SPF rooms and adjacent areas.
4. All cages are autoclaved after being washed and just prior to being returned to colony rooms. Cages must not be interchanged between "SPF" and "conventional" colony rooms.
5. All inanimate objects (cages, feed cans, refuse cans, etc.) enter or leave each colony room via a steam lock.
6. Caretakers are required to completely change clothing and to observe other very strict regulations upon entering or leaving colony rooms through specialized personnel locks. Only the most skillful and dependable caretakers are selected for these positions.
7. A testing protocol must be established to determine the presence or absence of selected infections in the colonies and of any changes which occur in this regard.
8. Concomitant with the installation of SPF facilities in the production area must be the development of similar facilities in the laboratory areas. Otherwise, animals issued and held in "conventional" quarters would very quickly acquire "conventional" infections and the advantages of SPF production would be quickly voided—except possibly for animals used in very short-term experimental procedures.

RESEARCH FACILITIES CONSTRUCTION AND SITE ACQUISITION

1962 appropriation estimate, $2,800,000

Title to a farm was acquired by the Federal Government in May 1960 to be used by the National Institutes of Health for animal research and production purposes. The farm will be operated by the Division of Research Services which serves as a source of supply of animals used by the several Institutes and Divisions in research and also for the long-term holding of animals under observation for research purposes. Added facilities on Government-owned property outside of Bethesda were required for the following reasons: (*a*) Continuing increase in the number and variety of animals and animal types needed for research; (*b*) an increasing proportion of animals under long-term holding (1 to 5 years); (*c*) insecurity of limited space used at Casey farm, formerly the NIH farm; (*d*) overcrowding of laboratory aids branch animal facilities at NIH-Bethesda.

Further needs for space and facilities at the new farm which have developed since then comprise:

(*e*) Developing need for increasing the length of the quarantine period for dogs from 2 weeks to 4 weeks due to the deteriorating quality of these animals which are obtained from commercial sources, with proportionate increase in the laboratory aids branch dog population.

(*f*) Termination of the contract with Casey farm on July 1, 1960.

(*g*) Major increase in additional research facilities at the Bethesda reservation which will have the effect of accelerating the growth rate of animal populations needed for research (newly authorized Cancer Institute, Institute of Mental Health, and Neurological Diseases and Blindness Buildings, in addition to the previously known new Dental Institute and Biologic Standards Buildings).

The principal effect of these new developments on the planning of facilities needs and construction at the new farm has been to advance the schedules of animal population occupancy. This is especially applicable to dogs and cats. In a previous timetable, it was estimated that by 1965 a total of 500 dogs and 500 cats would be kept at the new farm. These two species, which use kennel facilities in common, amount to a dog population equivalent of 750 animals. It is now expected that this value will be reached by 1963. It is also anticipated that there will be some stepping up of the 1961–62 and the 1965 values of farm-type animals. These animals are kept in shelters and stalls.

In the breakdown of costs which follows, provision has been made in fiscal year 1962 for—

(1) Construction of utilities, perimeter fencing and tree planting, water supply, sewerage, incinerator, waste chemicals disposal, telephone, electric power and distribution, heating and air conditioning, roads, parking and loading space—all mainly staged construction	$935,575
(2) Construction of two functional buildings as follows:	
(*a*) A kennel building with service wing for dogs and cats. This building will have a population saturation value of 600 dog-equivalents, in runs and a normal occupancy value of 460 dog-equivalents. There will also be cages in the sick bays for 250 dogs or 250 cats	930,000
(*b*) A barn building with service wing. This building will provide shelter on an intermittent basis and feed storage for the 335 farm-type animals formerly scheduled for 1965 and now advanced in time. The buildings will have facilities ancillary to research and for treatment in the service wings (such as for the initial processing of specimens, bleeding, isolation, surgery, autopsy, etc.)	249,200
(3) Planning and design funds to complete design for fiscal year 1962 construction and for fiscal year 1963 construction	323,425
(4) Contingencies for 1962 planning and construction	361,800
Total	2,800,000

CONSTRUCTION OF GENERAL OFFICE BUILDING NO. 2

1962 appropriation estimate, $700,000

The general office building now under construction will be available for occupancy in the first quarter of 1962. At the time this structure was being designed, the proposed size was planned to permit relocating on the Bethesda reservation all NIH staff then located in rented space. However, programs have continued to grow during this interval, and it is now estimated that it will be necessary to continue to house about 1,000 employees in rented space when the general office building is occupied.

The National Institutes of Health has utilized rented space over an extended period of approximately 5 years. The experience during that time demonstrates the impracticability of continuing this practice on a permanent basis. Even at premium prices, office facilities properly designed for NIH functions are not available in nearby areas. The use of substandard office space and makeshift arrangements in structures designed as apartment dwellings results in inefficiencies which are not only expensive, but also serve as a deterrent to effective operations. Separating programs from the parent organization and from each other creates many problems of communication and program direction and results in additional expenses for servicing. These are real costs in addition to the identifiable rental charge currently averaging $600,000 annually.

The circumstances dictate the need for planning and constructing a second office building on the Bethesda reservation. It is proposed, therefore, to begin planning in 1962 for a facility with space to house approximately 1,400 employees. A structure of this size will permit some space for adjustment as a result of possible future growth or for the relocation of office staff presently housed in areas which could be converted to research laboratories should the need arise. Total planning and construction time is estimated at 3 years. The $700,000 in planning funds requested in this budget would permit planning to be started early in 1962, with construction to begin about midyear in 1963. Construction costs for this facility are currently estimated to approximate $10 million.

MIDDLE AMERICA RESEARCH UNIT HOUSING

1962 appropriation estimate, $400,000

The lack of housing facilities available to NIH personnel stationed at the Middle America Research Unit in the Canal Zone has been a continuous problem since the establishment of the Unit. The only housing officially assigned to the Public Health Service by the Canal Zone Government consists of two substandard units rented from the Panama Canal Company and inconveniently located some 20 miles from the laboratory. Practically all officers and civilian employees must domicile in the Republic of Panama as there is no available rental housing in the Canal Zone. This has created a hardship on all of the staff of the Middle America Research Unit. Those of the staff assigned quarters in the Canal Zone are inadequately and tenuously housed and must commute long distances, while those who live in the Republic must pay exorbitant rents.

At the present time, living quarters are required for 12 staff members and their families. The Canal Zone Government has offered to make available at no cost adequate building sites adjacent to a site now being prepared by the Federal Aviation Agency for housing units which are now under construction. The use of this adjacent site will result in a cost savings since it will be possible to tie into main roads and utility trunks which have been installed for the Federal Aviation Agency project. An appropriation of $400,000 is requested to develop land, and plan and construct 6 duplex family quarters, consisting of six 2-bedroom units and six 4-bedroom units.

This cost estimate was developed through consultation by representatives of the Institute of Allergy and Infectious Diseases with representatives of the Federal Aviation Agency at the Canal Zone. The cost for construction is expected to average about $22,250 per unit. Clearing of land, landscaping, roadways, sewers, and other utilities are estimated at $113,000, and planning, specifications, and supervision at $20,000.

CONSTRUCTION OF MASTER UTILITIES EXTENSION

1962 appropriation estimate, $645,000

The operating utility resources will reach their capacity with the completion of structures presently under construction at the National Institutes of Health, Bethesda, reservation. Extensive advancements to the central utility resources are now necessary to insure that there will be an adequate system available to service additional proposed structures.

With the completion of a master utility survey by Nottingham & Associates, management-engineering consultants, a detailed outline of requirements for the central utility resources has been developed to serve all additional structures presently plotted on the NIH master plot plan. Their recommendations indicated that there is an urgent need to (1) revise and expand our electrical system to provide additional capacity and flexibility, (2) make extensive alterations to the master fire alarm and watchman report system, and (3) construct a second steam line to the clinical center (building 10). It is estimated that $7,420,000 will be required for the planning and constructing of the total project.

A total of $645,000 is requested in 1962 for the design and planning of the entire system ($610,000) and for the construction of the steam line from the central main to building 10 ($35,000). Due to the complexity and diversity of the engineering features involved and due to the continued expansion of the National Institutes of Health, funds are requested at this time for the development of engineering plans for the entire system. A piecemeal approach to this project over several years would result in a more complex and more costly system.

Approximately 1 year will be required to complete the planning and design for the additions to the utility system, while it is estimated that the construction will cover a span of 2 years. The steam line construction is necessary in 1962 to provide as quickly as possible standby capacity in the event of a major breakdown in the primary service line.

MIDDLE AMERICA RESEARCH UNIT

Mr. Fogerty. The Middle America Research Unit is requesting funds for 12 houses; that is about $33,000 a house. Why is it so costly?

Dr. Shannon. This is an estimate that is based upon the experience of a very extensive housing development that has been underway by FAA over the last 12 to 18 months.

Mr. Fogarty. How does this estimate compare with FAA's?

Dr. Shannon. This is approximately the same as theirs. In other words, what we are taking is their estimate. These are duplex units which will have two and four bedrooms.

Mr. Doran. The construction cost is actually $22,250 on the average, and the site preparation and utilities account for the difference.

Mr. Fogarty. Doesn't one usually take into consideration the building site and the utilities?

Mr. Doran. It is part of the total cost; yes. But the construction itself—the $22,250—is not exceptionally high. For the Indian health construction quarters——

Mr. Fogarty. Mr. Denton.

Mr. Denton. Would you tell me just a little bit more about this Middle America Research Unit project.

Dr. Shannon. Yes, sir. This is a unit that was established approximately 4 years ago as a means of making available a research facility to study certain diseases indigenous to the middle America area and the United States, particularly the Southern States to the Gulf States.

This unit was set up in cooperation with the Army and the Navy. It parallels the activities of the Gorgas Memorial Laboratory, which is not in the Canal Zone but is in the adjacent city of Panama.

Up to the present time the studies that have been developed there relate primarily to viruses, particularly those viruses which are so-called arthropod borne—that is, having an inset as a transmitting agent. They cover such diseases as yellow fever which transcends the gulf area; the encephalitides which are in the western group west of St. Louis; and eastern equine encephalitis—those epidemic grain infections that are seen in the summer. Another area is that of general fungal diseases. It is not so much limited to those that are of concern because they are a nuisance such as the mycotic diseases of the skin, but rather the more serious ones that produce general infections.

This unit is staffed in part by Public Health Service personnel and in part by Army personnel, and is run under joint leadership. The Public Health Service staff is organizationally located in the National Institute of Allergy and Infectious Diseases.

Mr. DENTON. And this unit has been buying houses for the people who work in these laboratories?

Dr. SHANNON. At the present time about half of our personnel live in the city of Panama. The housing there is not only costly, but it is inadequate. In running a laboratory of this sort, at an offshore point, it is essential to have topflight personnel in residence to assure continuity of activity and productivity. We must have adequate housing available for the staff and their families.

Mr. DENTON. These houses cost about $22,250 apiece?

Dr. SHANNON. Yes, sir.

Mr. DENTON. How large are the houses?

Dr. SHANNON. I can't be sure, but as I recall these are two-bedroom and four-bedroom houses.

Mr. DENTON. Where do you have them in Panama—in the zone?

Dr. SHANNON. In the zone, yes, sir.

Mr. DENTON. But they work at the Gorgas Memorial Laboratory?

Dr. SHANNON. No, sir; they work in the Canal Zone.

Mr. DENTON. In the laboratories you have there?

Dr. SHANNON. Yes, sir.

Mr. DENTON. Didn't we increase the size of that Gorgas Memorial Laboratory?

Dr. SHANNON. Yes, sir; it is planned over the years to increase it slightly. This does not project any of that.

Mr. DENTON. I have been down there. It doesn't have adequate space for a laboratory. It is an old medical college, that's what it is.

Dr. SHANNON. You are speaking of the Gorgas Memorial Laboratory?

Mr. DENTON. Yes.

Dr. SHANNON. The Gorgas Memorial Laboratory received construction and renovation funds in 1961. As I said, this parallels the Middle American Research Unit, which is in the Canal Zone. The Gorgas Memorial Laboratory——

Mr. DENTON. Is in Panama?

Dr. SHANNON. In Panama, yes, sir. The space that we have for our unit there is in a converted nurses' home that is adjacent to the Gorgas Hospital. This space is working out very well.

Mr. DENTON. That is in the zone?

Dr. SHANNON. Yes, sir. But we feel we have taken care of the needs of the laboratory in the city of Panama through the construction funds that were made available in the last budget.

Mr. DENTON. That is all.

Mr. FOGARTY. Mr. Michel?

Mr. MICHEL. No questions.

Mr. FOGARTY. Thank you.

MONDAY, MARCH 20, 1961.

COMMUNITY HEALTH ACTIVITIES

WITNESSES

DR. THEODORE J. BAUER, CHIEF, BUREAU OF STATE SERVICES
DR. JAMES K. SHAFER, CHIEF, DIVISION OF COMMUNITY HEALTH PRACTICE
DR. ALBERT L. CHAPMAN, CHIEF, DIVISION OF ACCIDENT PREVENTION
DR. LESLIE W. KNOTT, CHIEF, DIVISION OF CHRONIC DISEASES
DR. CLARENCE A. SMITH, CHIEF, COMMUNICABLE DISEASE CENTER
DR. ARDELL B. COLYAR, OFFICER IN CHARGE, ARCTIC HEALTH RESEARCH CENTER
DR. DONALD J. GALAGAN, CHIEF, DENTAL PUBLIC HEALTH AND RESOURCES
MARGARET C. ARNSTEIN, CHIEF, DIVISION OF NURSING
STEPHEN J. ACKERMAN, FINANCIAL MANAGEMENT OFFICER, BUREAU OF STATE SERVICES
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	10, 896	12, 154	13, 029
	Positions other than permanent	1, 065	1, 380	1, 686
	Other personnel compensation	187	152	118
	Total personnel compensation	12, 148	13, 685	14, 833
12	Personnel benefits	1, 488	1, 664	1, 795
21	Travel and transportation of persons	1, 124	1, 288	1, 406
22	Transportation of things	219	231	261
23	Rent, communications, and utilities	315	335	344
24	Printing and reproduction	151	195	222
25	Other services	533	735	735
	Research contracts	826	1, 263	1, 242
	Payment to—			
	"Bureau of State Services management fund"	2, 024	2, 447	2, 618
	"National Institutes of Health management fund"	14	20	25
26	Supplies and materials	931	941	1, 001
31	Equipment	708	462	525
32	Lands and structures	1		
41	Grants, subsidies, and contributions	30, 657	35, 049	36, 745
	Subtotal	51, 138	58, 314	61, 751
	Deduct quarters and subsistence charges	−1	−1	−1
	Total obligations	51, 137	58, 313	61, 750

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	2, 020	2, 149	2, 282
Full-time equivalent of other positions	208	269	353
Average number of all employees	1, 995	2, 182	2, 402
Number of employees at end of year	2, 122	2, 393	2, 559
Average GS grade	6. 9	7. 0	7. 0
Average GS salary	$5, 705	$6, 102	$6, 071

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants to States for general health	14,985	17,000	17,820
2. Grants for public health training	2,923	4,430	5,000
3. Accident prevention	1,535	2,904	3,368
4. Chronic diseases and aging	1,119	1,386	1,998
5. Communicable disease activities:			
(a) Communicable Disease Center	7,921	8,466	9,271
(b) Control of venereal diseases:			
(1) Grants to States	2,372	2,400	2,400
(2) Direct operations	2,970	3,415	3,415
(c) Control of tuberculosis:			
(1) Grants to States	3,993	4,000	4,000
(2) Direct operations	2,467	2,493	2,493
(d) Arctic Health Research Center	463	532	508
6. Community health practice and research	1,801	1,952	1,961
7. Dental services and resources	1,822	2,133	2,182
8. Nursing services and resources:			
(a) Training grants	5,892	6,525	6,525
(b) Direct operations	705	768	810
Total program costs	50,969	58,402	61,750
9. Relation of costs to obligations:			
Costs financed from obligations of other years, net (−)		−89	
Obligations incurred for costs of other years, net	168		
Total obligations	51,137	58,313	61,750
Financing:			
Comparative transfers (−) from other accounts	−26,814	−31,178	
Unobligated balance lapsing	174		
New obligational authority	24,497	27,135	61,750
New obligational authority:			
Appropriation	24,497	27,120	61,750
Transferred to "Salaries and expenses, Office of the Surgeon General" (42 U.S.C. 226)		−142	
Appropriation (adjusted)	24,497	26,978	61,750
Proposed supplemental due to pay increases		157	

INTRODUCTORY STATEMENT ON COMMUNITY HEALTH ACTIVITIES

Mr. FOGARTY. The community health activities is next. Who is going to give the opening statement on that?

Dr. BAUER. Mr. Fogarty, I am going to make an introduction.

Mr. FOGARTY. All right; you go ahead.

Dr. BAUER. Mr. Chairman and members of the committee, I am happy to have the opportunity to appear before this committee on behalf of the programs of the Bureau of State Services. Our programs this year are being presented on a new appropriation structure. Instead of the separate appropriations that we have formerly used, we have grouped them into two consolidated appropriations, one for community health activities and the other for environmental health activities, with the major programs within this Bureau being presented in activities. I plan to introduce very briefly the community health activities, and Dr. Robert J. Anderson, who is the Deputy Chief of the Bureau of State Services, will introduce the environmental health activities.

The budget included in "Community health activities" actually supports the following operating divisions: Grants to States for general health, grants for public health training, and the community health practice program are all under the supervision of Dr. James K. Shafer, and he will make a statement concerning these.

Dr. Chapman will make a statement on accident prevention.

Dr. Leslie Knott, chronic diseases and aging.

Dr. Clarence Smith, communicable disease activities, which actually includes the Communicable Disease Center, tuberculosis, venereal disease control, and the Arctic Health Research Center.

Dr. Galagan, dental services and resources.

Miss Margaret Arnstein, nursing services.

Although this community health activities budget supports six divisions, in reality it supports three operating types of programs in health maintenance and disease and disability control; namely, chronic diseases, communicable diseases, and accident prevention.

GAP BETWEEN MEDICAL KNOWLEDGE AND USE

Working with the States and localities, all of these programs aim to reduce the gap that now exists between medical knowledge and its widespread use. It is clearly evident that knowledge, even in some of these well-established programs in communicable disease control, is not being fully applied. When you get around to the problems associated with chronic diseases, the gap between knowledge and its application is even more wide.

I think the principal reason for this gap is that the community patterns for providing health care have not kept pace with the growth and the age change in the population and with other sociological changes, including the change in the nature of the major health problems in the Nation.

Today we have in excess of 16 million people over 65 years of age. By 1970 this will increase 5 or 6 million. Three-fourths of these have chronic ailments of one sort or another. Ultimately, many of these older epople become more handicapped than they need to be, and ultimately they are likely to use much more hospital care than they or society can afford, unless more comprehensive health services are made available outside of the hospital.

OUT-OF-THE-HOSPITAL SERVICES

No community in the United States today has adequate out-of-the-hospital health facilities or services. Developing these, I think, is one of the most urgent needs in the Nation today. This has been recognized by the President in his health message when he stressed the need and called for legislation to provide grants to support and to stimulate the development of out-of-the-hospital facilities and services.

This need has also been recognized by a wide variety of professional groups, such as the American Public Health Association, State and territorial health officers, and the American Medical Association. They have developed committees and are working on this problem, not only by themselves, but with us.

With out-of-the-hospital services such as home nursing services, homemakers' services, physical therapy services, many patients could be cared for at home; and most of them would prefer to be there. With well-constructed and well-staffed nursing homes, many patients could receive the same adequate care they are now receiving in hospitals at a much lower cost.

To be effective, out-of-the-hospital services must be coordinated and to accomplish this, physicians, nurses, health officers, welfare workers, and a wide variety of other groups will need to work and plan much more together than they have in the past.

While I have been talking mainly about the chronic diseases and the aging problem in pointing up these new community needs, also important in the activities of community health activities estimates are programs providing for increased health protection to the other age groups, the children, and those under 65 years of age. Especially are these programs important in the communicable disease and in the accident prevention area.

If the Public Health Service is to give State and community help and leadership which is needed to work on these new coordinated patterns of health care, its own program needs to be coordinated by grouping all such programs together. In that way we can unify research, demonstrations, technical assistance, and other aids.

This is what we are attempting to do in this new structure within the Bureau, so that we can take advantage of a soundly balanced program and still promote each program to work as if theirs was the most important. All these services will be necessary if we are going to give a comprehensive health service program to the communities.

The budget estimate for all activities under "Community health activities" in this appropriation is $63,750,000, which represents an increase of $5,436,000 over the comparable figure of last year. Details of these estimates will be furnished by the program chiefs concerned, who are here this morning.

I will be glad to answer any questions.

SCOPE OF 1962 BUDGET CONSOLIDATION

Mr. Fogarty. This is a pretty large consolidation, isn't it?

Dr. Bauer. Yes, sir.

Mr. Fogarty. It is quite different from what we have had before. I don't quite understand it myself.

Mr. Denton. I don't either.

Mr. Fogarty. You made certain recommendations, didn't you, for consolidation and the Bureau of the Budget made others? Tell me the plans you made for consolidation.

Dr. Bauer. Essentially the programs represented under the budget proposal here under "Community health activities" covers the activities which were recommended by the study group of the Public Health Service; namely, bringing together those services that are services for the individuals in their health problems such as communicable diseases, chronic diseases, nursing and dental services with overall community organization to meet these services.

Then, too, although not shown in this appropriation, the study group of the Public Health Service recommended that the hospital or medical facilities be placed in this new grouping. This has been done; but the budget is still presented as a separate budget.

Mr. Fogarty. Is that the only difference between your recommendations and what the Bureau of the Budget sent to us?

Dr. Bauer. Originally our recommendations were that these major items be separate appropriations. They have been consolidated together under one appropriation and the activities have been so identified.

Mr. FOGARTY. Tell me how you presented it under individual appropriations.

Dr. BAUER. Under individual appropriations, essentially, sir, the activities now mentioned as shown on page 23 would have been separate appropriations rather than activities.

Mr. FOGARTY. You mean these eight?

Dr. BAUER. I believe that is true, is it not, Mr. Ackerman?

Mr. ACKERMAN. Yes, that is essentially correct.

Mr. FOGARTY. You mean you recommend that there be one appropriation for grants to States?

Dr. BAUER. Community health practices, which includes grants to States for general health; grants for public health training in item 6 would have been one—community health practices and research. Is this correct?

Mr. ACKERMAN. That is correct. The only combinations out of this were the grants and the community health practices.

Dr. BAUER. One, two, and six. The rest of them would have been separate.

Mr. ACKERMAN. Those are all administered by the same division.

Mr. FOGARTY. So there are going to be six presentations. Is that right?

Dr. BAUER. That is correct, sir.

Mr. FOGARTY. Why should we have six presentations if there are only three broad activities?

Dr. BAUER. I think it is necessary, sir—or at least desirable—because of the fact that activities such as nursing and dentistry need to be presented individually in order to bring out the special problems associated therewith.

VENEREAL DISEASES

Mr. FOGARTY. I can see offhand, I think, that by lumping all of these together some are going to sub-subactivities. Like venereal disease; I think it should be set out where people will notice it, especially since the incidence is going up and up. You are an old VD man, Dr. Bauer. What do you think about that?

Dr. BAUER. I think we are faced with a significant increase.

Mr. FOGARTY. It is going to get lost in here.

Dr. BAUER. As it relates to venereal diseases, there has been a significant increase in infectious syphilis the past 2 years, and in particular this past year. This is not only a reported increase; there is an actual increase manifested by the fact that our clinics in large cities are seeing more early syphilis than they have seen in a long time.

This is of great concern to us because, with the marked decrease in syphilis over a period of years, everyone accepted that it was going down, generally speaking. So this year, within the resources available, we have had to take a new trend in our whole operation and divert all our energies to infectious syphilis and also to working with the private physician, because he is the man who is seeing most of the cases, contrary to the fact in the older days they used to be seen mainly in public clinics.

Mr. **Fogarty.** I think last year your people told us that you were concerned because of the increase in the teenage group. Is that so this year?

Dr. **Bauer.** This is another disturbing factor, and that is early syphilis is occurring much more frequently than in the past in the early age groups; and also it is being seen in all social-economic groups. In the past it was mainly in the lower socioeconomic groups. Now it is still more prominent there, but it is being seen across the board as far as the economic groups are concerned.

PROGRAM GROUPINGS UNDER THE NEW APPROPRIATION

Mr. **Fogarty.** This is still confusing to me. For the record, at this point will you put in these three groupings. Then we will listen to the six presentations. Then I will see if I understand it any more clearly.

Dr. **Bauer.** Yes, sir.

The three groupings referred to are: (1) chronic diseases and related programs (grants to States for general health, grants for public health training, chronic diseases and aging, community health practice and research, dental services and resources, and nursing services and resources); (2) communicable diseases (Communicable Disease Center, control of venereal diseases, control of tuberculosis, and Arctic Health Research Center); and (3) accident prevention.

Mr. **Fogarty.** Who is the first witness?

Dr. **Bauer.** The first witness is Dr. James K. Shafer, who will present the grants to States for general health, grants for public health training, and community health practice and research.

General Statement on Improving Community-Level Health Services

Mr. **Fogarty.** All right, Doctor, go right ahead.

Dr. **Shafer.** Mr. Chairman and members of the committee, this statement covers those activities of the Public Health Service which are primarily concerned with the improvement of health practice and health services at the community level. In the budget document before you these are activity 1, "Grants to States for general health;" activity 2, "Grants for public health training;" and activity 6, "Community health practice and research."

Responsibility for these functions has been placed in a new Division of Community Health Practice with the objective of improving the availability, extending the scope, and insuring a high quality of health services to the people.

Expansion in availability of public health and medical care services will place existing health manpower and facilities under considerable pressure. Methods of health organization and administration which have been in existence for many years must be carefully reconsidered and revised to meet the needs of the present and future. They must be systematically studied and new methods devised, demonstrated and instituted.

The impact of programs upon individuals and communities must be evaluated and the findings must be translated into action through a high order of professional skill and much more effective selling of programs to the public. The present random organization of health services must be replaced by systematic plans that fit the needs of each community. Preventive, curative, and restorative services delivered through many separate sources must be integrated at the community level. Much needs to be learned about what determines individual and community behavior with respect to health. We must learn more about what will influence people to accept health facts and use available health services, and we must apply this knowledge to obtain the full application of our medical potential.

GRANTS TO STATES FOR GENERAL HEALTH

While other units of the Public Health Service are primarily concerned with the attack on individual disease entities or such essential health ingredients of our environment as water, air, and food, our Division's primary concern is with the effectiveness of the total health effort as it reaches people in their particular community setting. We are concerned with the structure of health organization, the methods by which services are delivered, the mechanisms by which quality standards are insured and the availability of essential health personnel, facilities, and services.

We strive to strengthen State and local organizations by assisting them to acquire the necessary knowledge and trained personnel to do the job. The general health grant, implemented by technical assistance provided through eight regional offices, is our basic tool. This grant, which is alloted among all of the States, is used to support basic State and community services and to inaugurate and strengthen new programs.

Among the fundamental health services which States use this grant to support are State diagnostic laboratories, environmental sanitation, health education, and public health nursing. Some of the newer activities which States have develeped with the help of this grant are services to improve the quality of nursing home care, accident prevention, occupational health, air pollution, chronic diseases and aging, and radiological health.

It is becoming increasingly important to assist the States and communities to maintain and strengthen these programs and to improve these services. In order to help States and local health communities meet the need for extension and improvement of these programs in the newer fields, such as radiological health, an increase of $820,000 is requested.

GRANTS FOR PUBLIC HEALTH TRAINING

No amount of effort to improve the organization and methods of delivering health services can hope to be successful, however, unless we also face up to the shortage of health manpower. The shortage of trained public health physicians, nurses, engineers, and other professional personnel and the need for retraining of presently employed personnel in new and developing fields constitute one of the most pressing problems in public health administration today.

We are striving to meet this need through a two-phase program—one to make it possible for students to receive training and the other to make it possible for educational institutions to provide it. Traineeships are awarded to persons who have already acquired basic professional qualifications which enable them to undertake graduate or specialized public health training. About 2,300 individuals were trained under this program in the past 4 years. With the $2 million available for 1961, approximately 625 more traineeships have been awarded. This represents awards to about one-half of the qualified applications which were received. This program will continue at the same level as in 1961.

The 12 schools of public health—an increase of 1 in the last year—constitute the principal resource for general professional public health training for all State and local health agencies. In order to provide these 12 schools with a cost of education allowance and to equalize the burden of their operating deficit between the States, $1 million per year is allotted among them on a formula basis. This program will continue at the same dollar level as in 1961.

In addition to the schools of public health, many of the schools of engineering and nursing also offer graduate or specialized public health training. In order to stimulate the development of training of the highest priority, grants on a project basis are made to these three types of schools upon the recommendation of an advisory committee of public health experts.

This program started in September 1960 and by the end of December we had received about 136 applications totaling $3,077,000 from about one-half of the eligible schools. The Advisory Council in the first 6 months has recommended approval of applications totaling $1,481,465, which is more than can be funded with the funds available for 1961. In order to bring this program into full operation at the authorized $2 million per year level, an increase of $570,000 is requested for public health training projects.

COMMUNITY HEALTH PRACTICE AND RESEARCH

The giving of expert advice and guidance to States and communities requires not only trained and experienced consultants but a constant source of new knowledge. To acquire this knowledge we will conduct and promote research into community health practices and services as a basis for more effective application of health knowledge. The growing problems of providing effective community health services in large cities and their surrounding metropolitan areas require special attention as the population of the United States becomes increasingly concentrated in such areas. The development of more effective methods of providing medical care services is one of the highest priority needs in order to assure that such services are more widely available, are of the highest quality, and are administered as efficiently and economically as possible.

In summary, we feel that the program operations supported from this appropriation represent some of the most challenging opportunities for extending and improving health services by—

Development, through research, of more effective public health practices;

Increasing, through training, of the numbers and capabilities of public health personnel;

Extension, through financial and technical assistance, of the scope, availability, and quality of community health services;

Giving special attention to the health problems of metropolitan areas and of agricultural migrants and to the improving of organization and administration of medical care services.

Mr. Chairman, I shall be glad to answer any questions that you may have about this program and the budget request.

DIVISIONS UNDER COMMUNITY HEALTH SERVICES

Mr. FOGARTY. I think we had better have the other two people give their statements. Is it two more?

Dr. BAUER. No, sir. There is one in accident; one in chronic disease and the aging; nursing; dentistry; and CDC—which will make five more.

Mr. ACKERMAN. Mr. Chairman, the point of this——

Mr. FOGARTY. Dr. Shafer just covered three, though.

Mr. ACKERMAN. All the others are discrete divisions, each other line. It so happens that Dr. Shafer administers these two grants and community health in this one division. So the three activities equal one division. All the rest are single division entities.

Mr. FOGARTY. I guess we will hear the rest of them, then, before we ask any questions. If this consolidation was for the purpose of confusing things, it is certainly a success.

Who is next?

Dr. BAUER. Dr. Chapman, Chief of the Division of Accident Prevention. He will speak to accident prevention.

General Statement on Accident Prevention

Dr. CHAPMAN. I have a short opening statement. Do you wish that read, sir?

Mr. FOGARTY. You can put it in the record, or read it—whatever you want to do.

Dr. CHAPMAN. If there are no questions, I had better read it and have it in the record.

Mr. FOGARTY. There will be questions.

Dr. CHAPMAN. I see. Then whatever your wishes are.

Mr. FOGARTY. You go ahead and read it.

Dr. CHAPMAN. Mr. Chairman and members of the committee, accidents for the most part are preventable occurrences. Their prevention depends upon the identification of causative factors, the development of measures to eliminate these factors, and the implementation of this knowledge through action programs.

The increased funds provided by Congress for 1961 have permitted substantial gains in the application of available knowledge as well as an extension in the amount of basic research being conducted.

EXAMPLES OF NEW PROJECTS IN 1961

A few examples of new projects financed by the increase for 1961 will serve to illustrate the potential of the accident prevention program.

In Connecticut a 5-year study has been developed to determine the relationship of disease and physical defects and motor vehicle accidents. In Cleveland, Ohio, the first "saturation" communitywide educational program is being conducted to determine whether such an intensive effort can save lives. In a rural area in Virginia another type of community organization is being undertaken in order to determine how to mobilize rural communities to the task of reducing the incidence of accidents. Results to date have been encouraging. There has been a 20 percent decrease.

In Arkansas, two public health advisors found that in a rural county fire deaths were due largely to faulty wiring and misuse of coal oil. An educational program brought about a rapid decline in the number of injuries. Such programs could be conducted in most rural areas throughout the country.

The national seat belt campaign was intensified. Films and TV spot announcements were produced. The use of seat belts in local, State, and Federal vehicles as well as in industrial fleets is growing steadily. Recently the automotive manufacturers have agreed to install fixtures in all 1962 automobiles for the front seat.

A "child proof" medicine safety chest was developed by the accident prevention program. It soon will be marketed. The poison control center is now conducting two pilot studies to demonstrate how to prevent poisoning in young children.

National conferences have been held, or are scheduled for the spring of 1961, in such areas as (1) cooperation between State health departments and motor vehicle administrators—there have been two of these so far; (2) simulation devices—we just completed that conference in Santa Monica last month; and (3) drinking and driving, which will be held in Pittsburgh in May.

Contracts have been let for applied research projects in such areas as: Analysis of the task of driving; simulation; role of human factors in accident causation; occurrence of accidents in children and old people; role of osteoporosis in hip fractures; "off-the-job" accident occurrence; and methods of motivating housewives to serve as home safety supervisors. These are but a few examples of a wide range of studies and investigations which are providing valuable information about the way the various types of accidents occur and how they may be prevented.

The growing recognition of the importance of the role of human factors in accident causation has attracted the attention and aroused the interest of physicians, public health workers, and many types of scientists.

These human factors can be studied in the same way that the causative factors of tuberculosis and the venereal diseases were studied. Preventive measures can be developed and applied by the medical and public health profession. The same type of research which is being done to determine the causes of cancer, heart disease, and stroke can be applied to determine the true causes of accidents. As a matter of fact, all of the traditional skills of medicine and public health, with relatively small modifications, can be used to bring about a reduction in the incidence of accidental injuries and deaths.

The aroused interest in accident research is indicated by the increasing demand for research grant funds. Grants for accident prevention research have increased from $83,000 in 1956, at which time the Public Health Service expanded its accident prevention program, to a level of $1,482,000 in 1961. There is evidence that requests for research grant funds will be increasing rapidly. The 1962 budget now before the committee provides for an increase of $439,000, for a total of $1,921,000. It should be noted that this is the first time that research grant funds have been carried in this activity.

ROLE OF PHS IN ACCIDENT PREVENTION

In discussing the role of the Public Health Service in the area of accident prevention, I would like to refer back to the House committee report on the 1961 appropriation bill. The report stated:

> The Surgeon General's report on environmental health described the activities of official health agencies in the accident prevention field as falling "far short of meeting the need for effective measures to reduce the toll taken by accidents particularly among children."
>
> This opinion received strong concurrence from an outstanding expert in the field who appeared before the committee. With accidents the No. 1 cause of death for children and young adults in the prime of life, the lack of emphasis in this field cannot be condoned. The bill, therefore, includes an increase of $1 million to permit the Public Health Service to initiate an effective well-balanced program.

This report stands as a landmark in promoting the mobilization of public health resources in the attacks on death and disability due to accidents. Now after decades of dormancy, the health professions have reacted constructively to the challenge of accident prevention. Researchers are turning in growing numbers toward work in this field. Health departments and physicians have found a role to play and in the years ahead will, as leadership and resources are provided, make notable contributions to accident prevention.

However, many tasks remain to be done in the years ahead in addition to broadening the search for the causes of accidents. Ways of applying currently available accident prevention "know-how" must be found; new types of training must be provided; cooperative efforts with other National, State, and local safety groups must be extended.

The 1962 budget request for this program is $3,368,000. It provides for essentially the same level of program operation as in 1961. The increase of $445,700 is primarily for additional research grants.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and budget request.

Mr. FOGARTY. Thank you, Doctor.

NEW ORGANIZATIONAL STRUCTURE

Mr. FOGARTY. Do you have legislative authority to set up an organizational structure to go with the recommended appropriation structure?

Dr. BAUER. As far as we have gone within our organizational structure, we have authority to break out this particular activity into a new bureau such as has been recommended by the study section. We would need legislative authority, yes. This is one of the two major activities in the Bureau of States Services at the present time, the other being environmental health.

Mr. FOGARTY. It is still a little controversial, isn't it?

Dr. BAUER. There are certain areas of this particular activity that have been mentioned as being controversial. One was that the report recommended that the mental community health services activity of the National Institute of Mental Health be transferred to this Bureau. This has not been done because of the concern of a variety of people.

But, generally speaking, in any of these areas that have been accomplished, there has been no controversy.

Mr. FOGARTY. Has the new administration approved the same legislative request to accomplish this reorganization that was sent to Congress last year?

Mr. KELLY. I don't believe it has been submitted as yet, Mr. Chairman. It is under consideration. There is every reason to believe it will be approved.

Mr. FOGARTY. This committee may not accept some of this proposed reorganization so far as the appropriations are concerned.

NEW LANGUAGE

What is the new language you have here?

Dr. BAUER. This new language actually is a clarification and bringing together of all the language as it relates to the activities brought under community health activities, and does not introduce, per se, any new language.

RECONCILIATION OF NEW WITH CURRENT APPROPRIATION STRUCTURE

Mr. FOGARTY. The tables beginning on page 122 of the committee print give a fairly good breakdown of everything that was in the bill last year as individual items, don't they?

Dr. BAUER. Yes, sir.

Mr. FOGARTY. So we will put the tables into the record at this point.

The President's budget proposes numerous transfers and consolidations within the overall Public Health Service budget. The following tables consolidate pertinent information regarding these adjustments.

TABLE A

This table shows the proposed appropriation structure and indicates, under each of the proposed appropriations, the transfers from current appropriations that will be made if the new structure is approved. Where no comparative transfers are shown, there is no change proposed in the activities to be covered by that appropriation item.

Reconciliation of proposed comparative transfers in 1962 budget

	1960	1961	1962
Buildings and facilities	$300,000	$3,776,450	$16,630,000
Community health activities:			
Base amount (assistance to States, general)	24,497,000	27,134,800	29,473,500
Add comparative transfers from—			
"Environmental health activities"		1,403,300	1,401,000
"Control of venereal diseases"	5,400,000		
"Control of tuberculosis"	6,452,000	6,493,400	6,493,400
"Communicable disease activities"	8,157,500	14,393,000	15,236,100
"Hospitals and medical care"	6,309,595	6,988,000	6,987,000
"Foreign quarantine activities"	151,508	161,200	162,000
"General research and services, NIH"	1,152,265	1,519,000	1,967,000
"National Institute of Dental Research"	1,911,697	2,092,700	2,182,000
Less comparative transfers to—			
"Environmental health activities"	−920,888	−62,100	−63,000
"Salaries and expenses, Office of the Surgeon General"	−135,709		
"National health statistics"	−1,548,922	−1,810,100	−2,089,000
Total on proposed basis	51,426,046	58,313,200	61,750,000
Hospital construction activities:			
Base amount (grants for hospital construction)	186,200,000	186,200,000	151,200,000
Add comparative transfer from "Salaries and expenses, hospital construction services"	1,650,000	1,736,000	1,772,000
Total on proposed basis	187,850,000	187,936,000	152,972,000
Environmental health activities:			
Base amount	15,720,000	27,942,700	32,488,000
Add comparative transfers from—			
"Community health activities (ASG)"	920,888	62,100	63,000
"General research and services, NIH"	4,270,247	5,686,000	7,366,000
"National Cancer Institute"	182,820	220,000	316,000
"Mental health activities"	72,242	158,000	236,000
"National Heart Institute"	496,979	704,000	968,000
"National Institute of Dental Research"	58,744	57,000	90,000
"Arthritis and metabolic disease activities"	220,021	345,000	432,000
"Allergy and infectious disease activities"	572,067	850,000	1,085,000
"Neurology and blindness activities"	96,711	191,000	217,000
Less comparative transfer to "Community health activities (ASG)"		−1,403,300	−1,401,000
Total on proposed basis	22,610,719	34,812,500	41,860,000
Grants for waste treatment works construction	46,816,000	45,000,000	50,000,000
Medical care and foreign quarantine:			
Base amount (hospitals and medical care)	51,600,000	55,823,000	56,319,000
Add comparative transfers from—			
"Foreign quarantine activities"	4,534,292	4,948,800	5,150,000
"Indian health activities"	45,773,991	50,271,000	52,430,000
Less comparative transfer to "Community health activities"	−6,309,595	−6,988,000	−6,987,000
Total on proposed basis	95,598,688	104,054,800	106,912,000
Construction of Indian health facilities	4,946,413	9,714,000	6 616,000
General research and services, NIH	45,994,000	83,900,000	96,737,000
Less comparative transfers to—			
"Community health activities"	−1,152,265	−1,519,000	−1,967,000
"Environmental health activities"	−4,270,247	−5,686,000	−7,366,000
Total on proposed basis	40,571,488	76,695,000	87,404,000
National Cancer Institute	91,257,000	111,000,000	109,608,000
Less comparative transfer to "Environmental health activities"	−182,820	−220,000	−316,000
Total on proposed basis	91,074,180	110,780,000	109,292,000
Mental health activities	68,090,000	[1] 95,761,000	83,158,000
Less comparative transfer to "Environmental health activities"	−72,242	−158,000	−236,000
Total on proposed basis	68,017,758	95,603,000	82,922,000
National Heart Institute	62,237,000	86,900,000	92,325,000
Less comparative transfer to "Environmental health activities"	−496,979	−704,000	−968,000
Total on proposed basis	61,740,021	86,196,000	91,357,000

See footnotes at end of table, p. 99.

Reconciliation of proposed comparative transfers in 1962 budget—Continued

	1960	1961	1962
National Institute of Dental Research	$10,019,000	$15,500,000	$15,307,000
Less comparative transfers to—			
"Community health activities"	−1,911,697	−2,092,700	−2,182,000
"Environmental health activities"	−58,744	−57,000	−90,000
Total on proposed basis	8,048,559	13,350,300	13,035,000
Arthritis and metabolic disease activities	46,862,000	61,200,000	62,671,000
Less comparative transfer to "Environmental health activities"	−220,021	−345,000	−432,000
Total on proposed basis	46,641,979	60,855,000	62,239,000
Allergy and infectious disease activities	34,054,000	44,000,000	45,370,000
Less comparative transfer to "Environmental health activities"	−572,067	−850,000	−1,085,000
Total on proposed basis	33,481,933	43,150,000	44,285,000
Neurology and blindness activities	41,487,000	[2] 49,600,000	49,683,000
Less comparative transfer to "Environmental health activities"	−96,711	−191,000	−217,000
Total on proposed basis	41,390,289	49,409,000	49,466,000
Grants for construction of health research facilities	30,000,000	30,000,000	30,000,000
Scientific activities overseas		3,707,000	10,084,000
National health statistics:			
Add comparative transfers from—			
"Community health activities (ASG)"	1,548,922	1,810,100	2,089,000
"Salaries and expenses, OSG"	1,473,674	2,236,200	2,553,000
Total on proposed basis	3,022,596	4,046,300	4,642,000
Operations, National Library of Medicine	1,566,000	1,738,000	2,066,000
Retired pay of commissioned officers	1,681,852	1,920,000	2,180,000
Salaries and expenses, Office of the Surgeon General:			
Base amount	5,816,000	7,368,100	7,828,000
Add comparative transfer from "Community health activities"	135,709		
Less comparative transfer to "National health statistics"	−1,473,674	−2,236,200	−2,553,000
Total on proposed basis	4,478,035	5,131,900	5,275,000
Construction of mental health-neurology research facility		12,139,000	
Total appropriations	841,262,556	1,038,327,450	1,030,987,000

[1] Does not include $5,139,000 transferred to "Construction of mental health-neurology research facility."
[2] Does not include $7,000,000 transferred to "Construction of mental health-neurology research facility."

TABLE B

This table shows the Public Health Service budget for 1962 as it would appear if no change were proposed from the appropriation structure of 1961, and compares these figures with the 1960 and 1961 appropriations.

Appropriations and estimates 1960–62

	1960 appropriation	1961			1962 estimate
		Appropriation	Supplemental	Total estimate	
Assistance to States, general	$24, 497, 000	$26, 977, 800	$157, 000	$27, 134, 800	$29, 473, 500
Control of tuberculosis	6, 452, 000	6, 430, 000	63, 400	6, 493, 400	6, 493, 400
Communicable disease activities	13, 557, 500	14, 116, 000	277, 000	14, 393, 000	15, 236, 100
Environmental health activities	15, 720, 000	27, 640, 000	302, 700	27, 942, 700	32, 488, 000
Grants for waste treatment works construction	46, 816, 000	45, 000, 000	------------	45, 000, 000	50, 000, 000
Grants for hospital construction	186, 200, 000	186, 200, 000	------------	186, 200, 000	151, 200, 000
Salaries and expenses, hospital construction services	1, 650, 000	1, 675, 000	61, 000	1, 736, 000	1, 772, 000
Hospitals and medical care	51, 600, 000	55, 213, 000	610, 000	55, 823, 000	56, 319, 000
Foreign quarantine activities	4, 685, 800	4, 931, 000	179, 000	5, 110, 000	5, 312, 000
Indian health activities	45, 773, 991	48, 276, 000	1, 995, 000	50, 271, 000	52, 430, 000
Construction of Indian health facilities	4, 946, 413	9, 714, 000	------------	9, 714, 000	6, 616, 000
National Institutes of Health:					
General research and services, NIH	45, 994, 000	83, 900, 000	------------	83, 900, 000	96, 737, 000
National Cancer Institute	91, 257, 000	111, 000, 000	------------	111, 000, 000	109, 608, 000
Mental health activities	68, 090, 000	[1] 95, 761, 000	------------	[1] 95, 761, 000	83, 158, 000
National Heart Institute	62, 237, 000	86, 900, 000	------------	86, 900, 000	92, 325, 000
Dental health activities	10, 019, 000	15, 500, 000	------------	15, 500, 000	15, 307, 000
Arthritis and metabolic disease activities	46, 862, 000	61, 200, 000	------------	61, 200, 000	62, 671, 000
Allergy and infectious disease activities	34, 054, 000	44, 000, 000	------------	44, 000, 000	45, 370, 000
Neurology and blindness activities	41, 487, 000	[2] 49, 600, 000	------------	[2] 49, 600, 000	49, 683, 000
Subtotal, NIH	400, 000, 000	547, 861, 000	------------	547, 861, 000	554, 859, 000
Grants for construction of health research facilities	30, 000, 000	30, 000, 000	------------	30, 000, 000	30, 000, 000
Scientific activities overseas	------------	3, 707, 000	------------	3, 707, 000	10, 084, 000
Operations, National Library of Medicine	1, 566, 000	1, 662, 000	76, 000	1, 738, 000	2, 066, 000
Construction of mental health-neurology research facility	------------	12, 139, 000	------------	12, 139, 000	------------
Buildings and facilities	300, 000	3, 776, 450	------------	3, 776, 450	16, 630, 000
Retired pay of commissioned officers	1, 681, 852	1, 920, 000	------------	1, 920, 000	2, 180, 000
Salaries and expenses	5, 816, 000	7, 042, 200	325, 900	7, 368, 100	7, 828, 000
Total, Public Health Service	841, 262, 556	1, 034, 280, 450	4, 047, 000	1, 038, 327, 450	1, 030, 987, 000

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[1] Does not include $5,139,000 transferred to "Construction of mental health-neurology research facility."
[2] Does not include $7,000,000 transferred to "Construction of mental health-neurology research facility."

INCREASE IN GRANTS FOR GENERAL HEALTH ACTIVITIES

Mr. Fogarty. Your first increase is $820,000 for "General health activities." What is that for?

Dr. Shafer. The $820,000, Mr. Chairman, will be an increase in the general health appropriation which will be used by the States in further expanding the gains made by increases in this general health grant last year. They were principally nursing home activities.

Mr. Fogarty. You had an increase last year of $2 million. Is that correct?

Dr. Shafer. That is correct, sir. This $820,000 will permit them to continue expanding their State or local health department staffs to follow promising leads in health improvements in their States.

Mr. Fogarty. Is it left up to the health officer of that State as to how to spend it?

Dr. SHAFER. Yes. He will receive this share of this increase according to our general health grant formula; and utilization of these funds is at the discretion of the State health officer. He simply submits a plan and indicating how he will use these funds. This is in turn approved by the Public Health Service.

Mr. FOGARTY. Have you ever had any trouble with the States not living up to these plans submitted and approved by the Public Health Service?

Dr. SHAFER. We do have exceptions to plans that are picked up by the auditors who go into the States following utilization of these funds. Generally we have found them to be of a very minor nature. The States do tend to follow the plan that they have submitted to the Public Health Service. We have had no major problems with the States.

IMPROVEMENT OF NURSING HOME CARE

Mr. FOGARTY. How are you spending the $2 million increase you received last year?

Dr. SHAFER. This $2 million increase, was directed specifically to improvement of nursing home care. We have had very encouraging reports from all the States on how they are actually using these funds at the present time. They have employed about 157 full-time workers and about 43 part-time workers up to the present time. These are principally in the nursing, nutrition, physical therapy, and rehabilitation categories, although we have added sanitation personnel in some States.

They are making a very broad attack on improving the care that is provided in nursing homes.

Mr. FOGARTY. What has Rhode Island done along this line?

Dr. SHAFER. As I recall, Rhode Island's increase amounted to about $8,700. They have employed one additional nurse, who is working with the department of welfare in the State of Rhode Island, because in this State the department of welfare has responsibility for licensing of nursing homes.

Mr. FOGARTY. Where do you think it ought to be—in the department of welfare or the health department? I am not talking about Rhode Island, but generally.

Dr. SHAFER. Yes. In the bulk of the States nursing home operations are licensed and supervised by State health departments. So I feel this is probably the best way to do it.

Mr. FOGARTY. It is an enormous job, isn't it?

Dr. SHAFER. Yes, sir.

Mr. FOGARTY. And you think they are making some headway?

Dr. SHAFER. We feel they are making real progress in getting staffs to work on these problems in nursing homes. They still need improvement.

Mr. FOGARTY. There are still a lot of problems.

Dr. SHAFER. Yes, there are.

Mr. FOGARTY. Do you think the accreditation program that was developed by the operators on their own will be of any help?

Dr. SHAFER. Mr. Chairman, I am not familiar with that program. Dr. Knott and his staff have been working on this particular program, and I feel he could answer that question far better than I could.

INCREASE IN GRANTS FOR PUBLIC HEALTH TRAINING

Mr. FOGARTY. There are three parts to the next activity, which is "Grants for public health training." Who will describe these and tell us how much is budgeted for 1961 and 1962?

Dr. SHAFER. Those are part of my division's responsibilities, Mr. Chairman.

Mr. FOGARTY. Go right ahead.

TRAINEESHIPS

Dr. SHAFER. The $5 million item includes $2 million for continuation of the title I traineeships to individuals, the same as in fiscal year 1961. There is an additional $1 million for formula grant support to the 12 schools of public health in this country.

Mr. FOGARTY. Will you put in the record the names of these schools and where they are located.

Dr. SHAFER. Yes, sir.

Columbia University, School of Public Health and Administrative Medicine, 600 West 168th Street, New York, N.Y.

President and Fellows of Harvard College, Harvard School of Public Health, 55 Shattuck Street, Boston, Mass.

The Johns Hopkins University, School of Hygiene and Public Health, 615 North Wolfe Street, Baltimore, Md.

Tulane University of Louisiana, School of Medicine, Tropical Medicine and Public Health, 1430 Tulane Avenue, New Orleans, La.

University of California, School of Public Health, Berkeley, Calif.

University of California at Los Angeles, School of Public Health, Los Angeles, Calif.

University of Michigan, School of Public Health, Ann Arbor, Mich.

University of Minnesota, School of Public Health, 1325 Mayo Memorial, Minneapolis, Minn.

University of North Carolina, School of Public Health, Box 229, Chapel Hill, N.C.

University of Pittsburgh, Graduate School of Public Health, Pittsburgh, Pa.

University of Puerto Rico, School of Medicine, San Juan, P.R.

Yale University, Department of Public Health, 310 Cedar Street, New Haven, Conn.

GRANTS TO SCHOOLS OF PUBLIC HEALTH

Dr. SHAFER. This $1 million support is continued at its current level. The remaining $2 million is for project grants to the schools of public health and schools of nursing and schools of engineering. This item was $1,430,000 during this current year, which is the first year of this project grant program.

The $570,000 increase would bring us up to the authorized ceiling of $2 million in this particular appropriation.

Mr. FOGARTY. What limit is placed on appropriations for these activities by the authorizing legislation?

Dr. SHAFER. The project grant appropriation is limited by legislation to $2 million. We hope to reach that ceiling in 1962. The $1 million for formula grant support to the schools of Public Health is the maximum authorized by current legislation. There is no legislative ceiling on the annual appropriations for title I traineeships.

APPLICATIONS FOR PUBLIC HEALTH TRAINING GRANTS

Mr. FOGARTY. You say in the justifications that you have about twice the number of qualified applicants than you have money to pay for.

Dr. SHAFER. That is correct, sir. That has been our experience over the last 4 years of this program.

Mr. FOGARTY. Is it going up or going down, or staying just about the same?

Dr. SHAFER. The number of applications seems to remain about the same.

Mr. FOGARTY. It seems to me I have more and more writing to me that there are no funds.

Dr. SHAFER. That certainly would be the experience we would expect, because we do restrict the applicants to those who are comparatively new in public health, who are below the age of 45 and who have not had previous training in public health. So we definitely limit the number of people eligible to apply for training.

Mr. FOGARTY. Are you against people because they are above 45?

Dr. SHAFER. Our national advisory committee felt that, with only $2 million available, we had to place restrictions on the applicants. This was a limitation that they proposed. Actually about 1.5 percent, of our applicants, who have been approved for training, have been approved as exceptions because they are over 45 years of age.

Mr. FOGARTY. So there are some pretty good people over 45?

Dr. SHAFER. There definitely are, sir.

HISTORY OF BUDGET REQUEST FOR TRAINING

Mr. FOGARTY. What did you ask the Department for?

Dr. SHAFER. As far as this training item was concerned, we asked the Department for $3 million for title I traineeships, which would have been an increase of $1 million. Of course the $1 million for formula grant support of the schools of public health was the same. We were also limited by the ceiling on the project grant authority.

Mr. FOGARTY. What did the Department ask the Bureau of the Budget for?

Mr. ACKERMAN. The total of this amount was $6 million. The Department's request was $5 million.

Mr. FOGARTY. The Department cut you back $1 million?

Dr. SHAFER. That is correct, sir.

Mr. FOGARTY. That is what the Bureau of the Budget allowed?

Dr. SHAFER. That is correct.

Mr. FOGARTY. It seems to me with this demand for training, this is one area where we ought to be spending a lot more than what we are.

Dr. SHAFER. We have discussed this with the schools, and they have indicated they could handle the additional student load.

Mr. FOGARTY. You couldn't have made a very good case before the Department, then, if they cut you back $1 million.

Mr. ACKERMAN. We tried, sir. This budget process is a very complicated thing. There are so many programs, so many areas to be covered, and many things are settled on the basis of overall policy.

Mr. FOGARTY. I am talking about this individual item. Don't you think they should be spending more money in this area?

Mr. ACKERMAN. We thought so because we asked for it.

Mr. FOGARTY. Do you still think so?

Mr. ACKERMAN. Yes, sir.

INCREASE FOR ACCIDENT PREVENTION

Mr. **Fogarty**. Why did you take "Accident prevention" out of "Environmental health"?

Dr. **Bauer**. This "Accident prevention" was moved from "Environmental health" to this appropriation because, after a very careful study by the study group, it thought that accident prevention belonged more in the sphere of operation of personal health services. This was a decision made by the Public Health Service.

Mr. **Fogarty**. You have an increase in that this year of $400,000-plus?

Dr. **Chapman**. $445,700 for research; none in direct operations, sir.

Mr. **Fogarty**. All in research?

Dr. **Chapman**. Yes, sir.

Mr. **Fogarty**. What kind of research?

Dr. **Chapman**. Basic research of the NIH type to be granted to qualified applicants.

Mr. **Fogarty**. This is not direct operations?

Dr. **Chapman**. No, sir; not to direct operation contract money. We don't have an increase in that area.

Mr. **Fogarty**. Did you ask for an increase?

Dr. **Chapman**. Yes, sir.

Mr. **Fogarty**. How much did you ask for? What did you ask the Department for?

Dr. **Chapman**. We asked the Bureau for $4,156,000. The Office of the Surgeon General recommended $4,156,000. The Department recommended $3,834,000. The Bureau of the Budget recommended $3,368,000—which is an increase of $445,700 in basic research.

Mr. **Fogarty**. The Surgeon General went along with your recommendation, but the Department cut it down?

Dr. **Chapman**. Yes, sir.

AUTOMOBILE ACCIDENTS

Mr. **Fogarty**. Even though accidents are going up. How many people were killed last year in automobile accidents?

Dr. **Chapman**. 38,000, Mr. Fogarty. The number remains fairly stationary from year to year. The rate per million miles traveled has gone down some, but the number of people killed per 100,000 population remains fairly stable. So the total number, with an increase in population and a decrease in mileage rate, keeps it at about 38,000 a year.

Mr. **Fogarty**. It is going to stay that way, too, unless the Department goes along with some of these requests and the Bureau of the Budget sees the light. I was hoping that since we have a new Secretary who made such a record in traffic safety as Governor in Connecticut that this would be one area where he would really go forward. But this is the best you can do?

Dr. **Chapman**. Yes, sir.

DRIVING SIMULATOR

Mr. **Fogarty**. What happened to the driving simulator?

Dr. **Chapman**. We had a very interesting conference in Santa Monica last month, in February, where experts in simulation, aviation and other types of military simulation, attended. They broke the conference down into three sections: The interests of the driver; the vehicle; and the highway.

The results were unanimous in the sense that there was a feeling that this was one important method of determining the basic human factors which are involved in accident causation on the highway which could be explored without risking people's lives in actual driving situations.

This report will be out in about 2 months. This was sponsored by the Automotive Safety Foundation, the Bureau of Public Roads, and the Public Health Service. We have let one small contract with a Connecticut research group who didn't do simulation using an automobile, but they did it on drivers doing highly skilled tasks. They would keep them up 24 hours, for example, and sit with them to see that they stayed awake. They found there was a tremendous decrease in the efficiency of doing prelearned tasks after they had been awake 24 hours.

You can see the implications this has on a man driving on a throughway who has been up for 24 hours. Several of them went to sleep and they couldn't even wake them up when flash bulb pictures were taken.

They also tested the antihistamine drugs, various tranquilizers, alcohol, and so forth. This is a crude attempt to evaluate these factors to point up what we could do using a true driving simulator.

While out in Santa Monica, I went through the UCLA simulator which uses motion pictures and is just one-third of the way toward completion. I was amazed that some of the people who got in that simulator actually got carsick—the illusion was so great. They can simulate the motion of the car, speed, and so forth. But until they get true high-fidelity simulation, they can't translate this into the actual driving situation.

Mr. Fogarty. What are you going to do with the results you have been getting out of this study in Connecticut?

Dr. Chapman. We are going to publicize them, sir, and hope that it will stimulate interest and knowledge about simulation, which is very scanty, even amongst the professional groups. That was the trouble when we talked about a simulator 2 years ago. As you know, it was proposed in 1960, 1961, and 1962. Nobody quite knew what we were talking about when we said a simulator.

So by holding a simulation conference, it got a full page in the Herald Tribune, for example; and eventually it will appear in professional journals, medical journals, trade journals, safety journals. When this knowledge of the value of simulation permeates throughout professional circles and down to the people, I think the answer will be obvious.

Mr. Fogarty. You know there has been a controversy as to who should bear the expense of that—the highway program or the Public Health Service. Many of us thought private industry ought to do quite a bit.

SEAT BELTS

You said the automobile industry has agreed to put seat belts in the front seats of all new cars.

Dr. Chapman. Yes, sir. In a recent news release the president of one of the larger automobile companies said the safety features which had been incorporated in automobiles in the past 50 years had been largely the result of industry stimulation. They have changed their policy and are now going to highlight safety. Another large manufacturer followed suit shortly thereafter and the other car manufacturers are cooperating.

So they are changing their mind now on the importance of safety.

Mr. Fogarty. I think they could do a much better job than they are doing.

Dr. Chapman. I did ask the folks out at UCLA, who had this partly developed simulator, how quickly they could complete a high fidelity simulator if there were no funding problems, and they said in approximately 2 years. So the technical know-how does exist.

FREQUENCY OF ACCIDENTS AND ACCIDENTAL DEATHS

Mr. Fogarty. You say on page 43:

> Accidents rank fourth in the leading causes of deaths in the United States. For the age groups 1 through 34 they are the leading cause of death.

Is that so?

Dr. Chapman. Yes, sir; 55 percent of all deaths from age 15 to age 24 are due to accidents.

Mr. Fogarty. This says 34.

Dr. Chapman. The 55 percent is for all accidents. Thirty-seven percent are due to auto accidents. Fifty-five percent of all who die die an accidental death—5.5 out of 10 youngsters.

Mr. Michel. What age?

Dr. Chapman. Fifteen to twenty-four. The other remarkable thing is in the aging group—the aging only make up 9 percent of the population, but 75 percent of all fall deaths are in over-65-year-old people. Thirty-three percent of the pedestrians killed are over 65, and 25 percent of the people who are killed by fire are over 65 years of age.

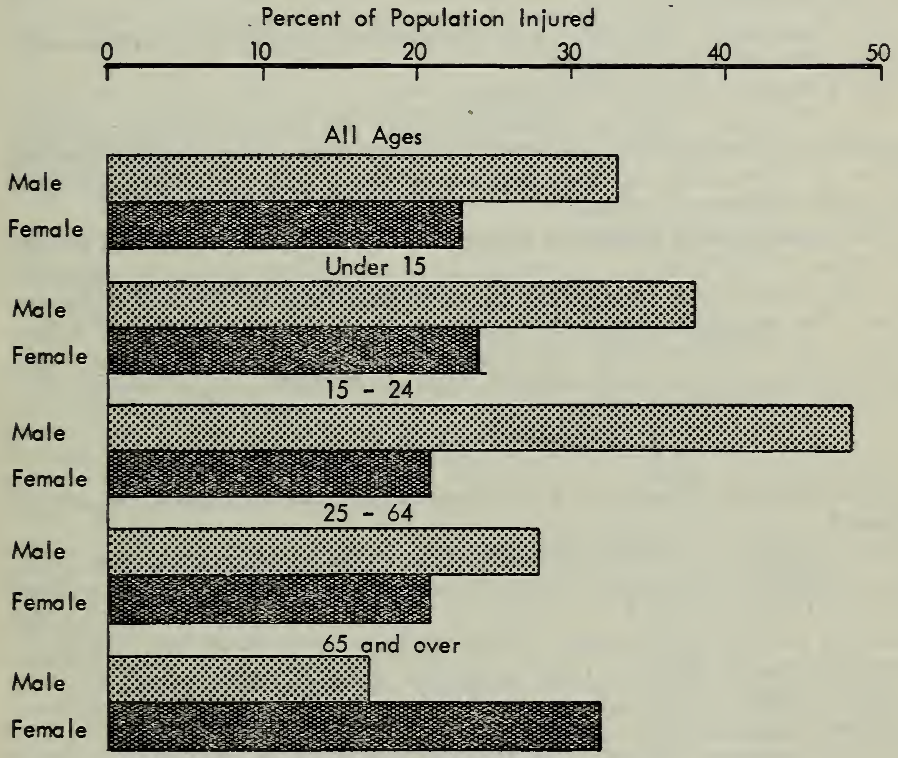
So there is a great need to concentrate on this over-65-year-old age group. A study is planned in a Detroit hospital on osteoporosis. There is an interesting chart here which shows that the only time when female injuries from accident exceed male injuries is in the over-65 group. I have got it here someplace.

Mr. Fogarty. Put it in the record.

(The chart referred to follows:)

ACCIDENTAL INJURIES IN THE UNITED STATES FISCAL YEAR 1958

(NUMBER OF PERSONS INJURED IN YEAR - 47,000,000)



Source: U.S. National Health Survey

DHEW-PHS Accident Prevention Program
Division of Special Health Services
January 1959

Dr. Chapman. After 65 the female injuries from accidents are double the male injuries. In every other age period they are the reverse. Dr. Smith out there is doing a study which shows that osteoporosis is a disease which tends to attack white women over 65. He believes he can prevent it if he can find the causes of it, whether this be a lack of calcium or a lack of hormones. That is what he wants to do, you see, is to prevent premature osteoporosis. These are not really accidental deaths. They are osteoporotic deaths.

HOME ACCIDENTS

Mr. Fogarty. With those figures, I can't understand why you weren't allowed more in your budget. The home accidents are still way up, aren't they?

Dr. Chapman. Yes, sir. The automotive accidents are more dramatic than the home category.

Mr. Fogarty. They get headlines.

Dr. Chapman. They get headlines, but the home accidents cause a majority of the injuries. One out of every three people in the United States is injured by an accident every year, and many of these are the result of home accidents.

The trouble with accidents is they aren't repetitive. If there were 100 cases of diphtheria, we would have a national campaign against it. But if you get 100 accidents, each one may be from a different cause—for example, you have to drive 18 million miles to get killed in an auto. So the study of accidents is a very difficult thing. The specific causes are not repetitive. So people tend to say, "Oh, well."

ACCIDENTAL POISONING

Mr. Fogarty. What are you doing about the accidents caused by poison?

Dr. Chapman. We took specific action in that area in order to stimulate industry to help out. Here is a picture of a safety medicine chest that the PHS patented. As a result of that, a meeting was held with industry several weeks ago. They already have been stimulated to develop three prototypes that are better than this one.

Mr. Fogarty. That is because of kids reaching up and taking these poisonous substances?

Dr. Chapman. Yes, sir. In the case of 55 percent of the children who ingest poisonous substances, the poisonous substances are medicines.

Mr. Fogarty. But your training program has remained the same?

Dr. Chapman. No, sir. This year we are letting a contract with New York University to develop a curriculum which will permit us, when the time is opportune, to train 50 accident prevention specialists a year over a period of 4 to 8 months and assign these men to local areas where there is a need for workers who are knowledgeable about the true cause of accidents. There they can take advantage of local situations, and develop accident prevention activities.

GENERAL STATEMENT ON CHRONIC DISEASES AND AGING

Mr. FOGARTY. Now we go to the next activity, chronic diseases and aging. Who is going to tell us about that?

Dr. BAUER. Dr. Leslie Knott, Mr. Chairman.

Mr. FOGARTY. You have an increase of $612,400 and 20 positions. Will you give us a breakdown of the positions and supply for the record what they are going to be used for.

Dr. KNOTT. Yes, sir.

(The information referred to follows:)

Ten positions will be located at headquarters. One GS–11, and two GS–9 statisticians will be involved in data collation. One GS–12 medical staff assistant, two senior assistant commissioned officers and one information specialist will direct the separate activities, care of the sick at home, etc. Two GS–5 and one GS–4 secretaries will assist the above-named professionals.

Ten positions will be located in the field. Four full grade nurse officers, three GS–12 public health program specialists and one GS–12 medical staff assistant will act as project officers and project developers for new cooperative projects. Two GS–5 secretaries will assist the professionals.

Mr. FOGARTY. Now give us a statement as to how you are going to use this $612,400.

Dr. KNOTT. Mr. Chairman, I have a full statement which I should like to submit for the record. I can then present a summary, if that is agreeable to the committee.

(The general statement follows:)

STATEMENT BY CHIEF OF DIVISION OF CHRONIC DISEASES

Mr. Chairman and members of the committee, there is little need to take the time of this committee to recite in detail the facts and findings regarding our national problems on chronic illness, disability, and the health of the aged. You and your committee colleagues have heard them many times, as evidenced by your deep concern over these subjects expressed on a number of occasions, most recently at the White House Conference on the Aging. Data are available to give us all the evidence we need to appreciate and understand the size and the seriousness of the problem. The main consideration in chronic disease control is not the magnitude of the problem, which we all recognize. The principal concern to the Congress, the Service, and the public is: What are we going to do about it?

It is true that we have not yet discovered the causes of most of the long-term illnesses which result in so much disability today. A sadder fact is that we do not have a vaccine or comparable procedure such as produced by the eminent Jonas Salk which can permit our people to escape the onset of such conditions as diabetes, glaucoma, arthritis, stroke, multiple sclerosis, cancer, and heart disease. These are types of problems which fully justify a continued, vigorous program of research. But these truths are not cause for wringing our hands in despair and waiting, because I assure you, Mr. Chairman, we do have the knowledge that can be applied to prevent much of the disability and dependency caused by these diseases, and even in the face of disability we do have the knowledge to minimize its effects and to provide the afflicted with a greater degree of independence, of comfort, and of hope. But the tragic part of the situation is that so little of this knowledge is being put into action. The reason for this may be that, in spite of the fairly widespread awareness of the problems and of methods of attacking them, the lack of adequate resources for developing action programs is just now being recognized.

A new division has just been organized on these problems and to develop new direct action programs that can help to meet some of the needs that exist today. This new division includes the cancer and heart disease control programs whose activities are financed through appropriations made to their respective institutes. Administratively they are an integral part of the Division of Chronic Diseases. They share in the development and conduct of the overall program for the chronically ill and the health of the aged.

The two fundamentals of this Division's programs are (1) prevention as applied to specific chronic diseases and (2) community health services needed for the effective care of the chronically ill and health of the aged. All of the Division's activities—its investigations, demonstrations, training and informational services, and technical assistance—are directed to furthering these two fundamentals.

PREVENTION

Prevention as applied to chronic disease today does not mean preventing the illness, but rather preventing progression of the illness, its complications, and impairment of bodily function. To illustrate this more concretely, I would like to call to your attention two unsolicited letters that recently came across my desk. One letter is written by a practicing physician and addressed to our medical officer directing a mobile disease detection unit in a State. It reads in part as follows:

"On November 12, 1960, a glucose tolerance test (a diabetes test) was done on one of my patients.

"The 2-hour reading of 130 mg. percent, of course, makes him a borderline case. Mr. M has been advised to be moderate in eating, and I think he will be. Certainly I see no indication of rigid dietary control. Thank you very much for your detection of blood sugar in this man, and for reporting it to me. He might well be a latent diabetic, and I hope that by exercising reasonable control he might keep himself from getting a more fully developed attack of the disease."

The second letter was written by a highway engineer to the State health officer in the same State.

"I was one who volunteered to participate in the accident prevention study recently conducted in the Hartford area.

"As a result of the physical examination I was referred to my family physician who in turn referred me to an eye specialist.

"The eye specialist concurred in the findings of the medical screening staff and concluded that I suffered from glaucoma. The disease is in its very early stages and constitutes a borderline case which can be effectively and successfully controlled by the use of drops.

"I should like to take this opportunity to offer my sincere and heartfelt thanks to all those people who conducted this survey as my doctor has informed me that this disease, allowed to go on undetected and untreated, could result in serious damage to my eyes."

These letters come from two thoughtful individuals who, without being asked, took time to express their appreciation. But with the thousands of apparently well people who undergo the tests for early detection of chronic disease, there must be innumerable, unwritten letters of thanks to those who have made early detection possible.

There has been gradual progress in developing diabetes screening programs in recent years. However, diabetes testing programs are now operating in only one-half of the States in the Nation, and some of them are on a very limited scale. All in all we are testing less than 1 percent of our total population. Our eventual goal is to screen at least 4 percent of the population each year, concentrating on those who have the highest risk—the obese, those over 40, mothers giving births to large babies, and persons having diabetic relatives.

The story of glaucoma control is similar. While acceptance of detection programs in this disease has been slow in developing, there is mounting evidence today of increasing recognition of the need for such activities. The instrument used to find increased fluid pressure in the eyeball requires more skill than testing for diabetes. We are searching for new techniques to overcome this difficulty. Limited glaucoma detection activities are now in operation in 20 States. Our job is to expand existing activities and start programs in the 30 remaining States.

Glaucoma, however, is only one segment of the problem of visual disability. Cataracts, diabetes, eye injuries as well as glaucoma account for 85 percent of blindness. Vision conservation, therefore, is the broader objective that must be pursued. To this end, we are planning regional and State conferences to bring together leaders and those who should be concerned with visual health. Our aim is to create a greater awareness of the problem and to stimulate action in developing programs for the prevention of visual disability.

We have already set our course for investigating in 1962 potentialities for prevention in other chronic disabling conditions. The entire field of hearing loss, its causes, prevention, and the necessary programs needed to conserve hearing function is a subject for pilot action in 1962. In this same year we shall intensify our efforts to find an appropriate test for the early detection of undiagnosed gout, because we know that the prophylactic use of a drug called colchicine can prevent acute episodes of this disease and the resulting joint damage. We are going to explore in depth the feasibility of developing preventive and control measures in such important disabling diseases as peptic ulcer, senility, allergies, kidney diseases, epilepsy, multiple sclerosis, and others. Preliminary conferences with colleagues in the National Institutes of Health indicate that possibilities do exist in some of these disease areas. By 1963 we hope that exploration will turn to application in those fields holding the greatest promise.

What I have been discussing thus far, Mr. Chairman, is early disease detection. Where possible, measures applied to single disease entities are combined in what are called multiple screening projects. These provide for a battery of tests including blood pressure, heart functioning, chest diseases, sight and hearing, blood testing for diabetes and venereal disease, and in some instances cancer detection. Such programs are operated with our support in several States. This type of procedure also forms a base for periodic health appraisal and counseling for the aged. So far comprehensive health appraisal programs exist only in a few places and are generally limited to welfare beneficiaries. We plan to conduct several pilot demonstrations in 1962 and evaluate their effectiveness in maintaining the health of the aged.

These are disease detection activities, but I should like also to mention another form of prevention, which is the restoration and preservation of bodily function and physical independence when disability already exists. Stroke with its 2 million victims, and arthritis with its 11 million sufferers are well known to all of us. Yet, with the application of relatively simple techniques, 60 to 80 percent of stroke victims who live can be restored to useful existence. The techniques are illustrated in the booklet "Strike Back at Stroke." A similar booklet "Strike Back at Arthritis," shows procedures that can preserve much function and prevent considerable deformity and disability. The Government Printing Office reports that "Strike Back at Stroke" is a best seller, and requests for the booklet on arthritis have already exceeded the initial publication. We are not content with such information; our concern relates to the extent of actual application of these measures to the victims of stroke and arthritis. Our recent study of the stroke program in Kentucky shows that physicians found the booklet extremely useful for a number of reasons: (1) It helped many patients to attain self-care; (2) it simplified the problem of teaching patients and family members how to administer exercise; (3) it helped improve the attitudes of patients and families; (4) in the majority of cases it lessened the time the physician needed to spend with patients. The majority of all physicians expressed the desire to have similar booklets treating other medical problems, and we explore the feasibility of developing similar measures for other conditions causing nerve, muscle, or bone damage.

In summary, what we mean by prevention is early detection of disease to avoid complications and disability, and the application of measures to preserve and restore physical ability when acute disabling disease strikes. We have made gradual progress, but we must bear in mind that only a small fraction of the population is receiving the benefits of knowledge that can be applied.

COMMUNITY HEALTH SERVICES AND NURSING HOMES

The second fundamental of the Division's activities relates to community health services including nursing homes, aimed at improving the care of the chronically ill and the aged. The services that are the targets of our concern cover a variety of activities:

Promotion and development of more home nursing service programs.
Expansion and improvement of homemaker services programs.
Development and extension of coordinated home care services.
Promotion and development of community information and referral service centers.
Improvement of care given to residents of nursing homes.

Community health activities such as these can provide adequate care and restoration in the patient's own home: they can bring service to those who do not need institutional care and in many cases cannot afford such care; they can enable the family to continue its normal activities with a minimum of disturbance to the household; they can bring new life and greater independence to the disabled and aged who would otherwise continue their days at home as burdensome invalids. These are the services of importance to all forms of disability whether they be heart disease, cancer, arthritis, senility, or other types of long-term disabling illness.

May I illustrate this more concretely by citing the actual case of Mrs. C., a Detroit resident.

Mrs. C, a 31-year-old mother of two very young children, suffered a stroke with complete paralysis of her right side and loss of speech. After 1 month of hospitalization, she was discharged to her home still in need of considerable care. Her physician, however, considered her prognosis for rehabilitation as good.

Her discharge to home was made possible because a community home nursing service was available. The nurse planned with the family for the assignment of a homemaker to assist in caring for Mrs. C, to care for her children, and to help Mrs. C in the care of the home.

Mrs. C, however, became quite dependent and evidence pointed to the need for considerable physical and emotional support if she were again to resume the role of mother and housewife as deemed possible by her physician. The nurse, physical therapist, occupational therapist, and homemaker, all part of a home nursing service, worked closely together to offer this patient a coordinated program of help. Under this plan the nurse assisted the patient in overcoming her fears and emphasized the importance of self-help. The therapists provided the technical assistance needed to conserve and strengthen muscle and joint function. Later, a speech therapist helped Mrs. C to learn again how to produce spoken syllables, words, and sentences. The homemaker's goal was to motivate the patient to care for herself and gradually to take over direct responsibilities for her home and children.

The homemaker remained in the household 5 days a week for a period of 6 months and gradually withdrew her services as Mrs. C gained increasing self-confidence and ability. By the end of 6 months, Mrs. C was able to speak adequately though with some difficulty. She was capable of taking complete care of her children and doing practically all the housework.

Mrs. C's situation had all the potentialities for a life of near-total disability, a disrupted home, and a prolonged burden on the family income. A community health service saved that family as it can numerous other families and individuals if community awareness of these problems is translated into community action.

It is this kind of action which the Division of Chronic Diseases is attempting to promote. It does this by providing financial assistance to get communities started, through informational and educational services and through other forms of technical assistance and guidance.

In some communities it may mean seizing an opportunity to organize a homemaker service or adding it to an existing agency. In still others, the provision of home nursing may be more feasible. Elsewhere we might find it practical to help develop a comprehensive home care project including physicians' services. Many communities could well utilize a central information, referral and counseling service that assists the chronically ill and the aged to obtain coordinated health care. What is accomplished depends upon the existing services, the needs and the nature of a community's problems and resources.

The paucity of existing services highlights this need for action.

In all of the United States:

Two hundred cities with populations of 25,000 and over have no visiting nurse service.

Less than 50 coordinated home-care programs are in existence, serving a mere 5,000 people.

One hundred seventy-five homemaker programs provide service to 3,000 families.

You can count on the fingers of both hands the number of communities having information and referral programs.

Currently we have on hand a substantial number of requests from States and communities for financial assistance to begin various types of community health service projects. These are all related to the care of the chronically ill and aged. This year we are unable to meet these requests.

Most of the increase requested in 1962 is designed to provide initial financial help and technical assistance to communities where such services do not now exist.

In addition our plan provides for continued help in the expansion of existing services, the evaluation of community health services, and the search for new ways to provide home care.

Another important activity of the Division is directed to improving care of the 500,000 persons, whose average age is 80, and who spend their lives in some 25,000 nursing homes in the Nation. This spring we expect to publish for use of State licensing agencies and other standard-setting organizations, a guide for developing minimum standards relating to administration of nursing homes, their physical facilities, and patient care. In 1962 we propose to continue our efforts in the following activities:

Strengthening working relationships between hospital and nursing homes;

Developing model record systems for nursing homes;

Organizing training courses for nursing home personnel in the care and rehabilitation of patients;

Improving nutritional services; and

Assisting State agencies in developing the kinds of programs that will help them to elevate the standards of care in nursing homes.

In carrying out these objectives we are working with a wide variety of organizations: Licensing agencies; welfare organizations; health departments; medical, nursing, and hospital authorities, as well as the nursing homes themselves and their National and State organizations. In developing the Standards Guide we sought and received advice and assistance from 61 people representing many different organizations.

We believe that the White House Conference on Aging, the recently enacted Medical Assistance Act for the Aged, and the concern expressed by the Congress not only reflect an increasing public awareness of the problem, but are strong evidence of a public demand and a public willingness to find the solutions in their States and communities. On our part we must provide the necessary answers to supply the new tools and methods and the leadership, stimulation, and support to States and communities in putting the established knowledge to work saving lives and preventing or ameliorating disability. In view of the magnitude of the problems and the current deficiencies in programs and services, we must move forward as rapidly as our capabilities and resources permit.

The budget as amended provides an increase of $2,572,400 for activities concerned with care of the sick at home and comprehensive community health services for the chronically ill and aged.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Dr. KNOTT. In speaking to this item in the appropriation, I don't think it is necessary to recite the facts and figures on the health of the aged and chronic diseases. I think you and your colleagues are fully aware of the problems. The question of concern to the Congress, to the people, and to the Public Health Service is: What are we going to do about it?

I should like to answer that question, if I may, in terms of the activities and the plans of the newly organized Division of Chronic Diseases, which was established to concentrate on the problems of chronic disease and the health of the aged. This Division includes administrative responsibility for heart disease control and cancer control programs which are financed through NIH appropriations, but which are integral parts of our Division.

The two fundamentals of the Division's programs and activities are, first, prevention as applied to specific chronic diseases; and, secondly, community health services needed for the effective health care of the chronically ill and the aged. These apply, Mr. Chairman. across the board to all sections of this Division.

PREVENTION OF CHRONIC DISEASES

Let us take the first of these—prevention. Prevention as applied to chronic disease does not, of course, mean preventing chronic illness, but rather preventing the progression of the illness, the complications, and the impairments to bodily function. Our primary goal in this respect is to discover disease conditions in the very early stages, when symptoms are minimal or even do not exist, but at a time when treatment can be most effective in preventing disability.

Currently, our major efforts are directed to two important chronic diseases under this particular appropriation. They are diabetes and glaucoma, two important causes of disability and two areas in which we have made gradual progress. Our experience has been that such pilot programs, once established, are enthusiastically received. But we are not content to remain with these. In 1962 we hope to explore with our colleagues in the National Institutes of Health various other diseases in which preventive measures can be developed and applied.

These are prevention programs based on disease detection. They, in conjunction with tests for cancer and examinations for heart disease, form a most important part of programs designed to provide health maintenance and health counseling for older people.

What we are trying to do in disease detection is to get at the problem before disability develops.

There is another form of prevention of equal importance, and that is the restoration and preservation of bodily function when disability already exists. The paralysis of stroke and the deformity of arthritis, I think, are familiar pictures to all of us around this table. Yet, Mr. Chairman, with the application of relatively simple forms of physical activity and exercise done under the guidance of a physician, the great majority of victims of these diseases can be restored to lives of usefulness and can be spared the disability and the degeneration so frequently associated with them. We hope to explore the usefulness of similar techniques and other conditions affecting bone, joint, and muscle.

I don't think I need to elaborate, Mr. Chairman, on the importance of the diseases which I have mentioned thus far with respect to their effect and the causes of disability and dependence among our senior citizens. They rank high as causes of disability and dependency in the age group 45 and above, and particularly those age 65 and over.

Prevention can do much to preserve the health of the aged if available knowledge along these lines were fully applied. Although we have made gradual progress, the unfortunate fact is that our available knowledge for preventing disability is not fully applied. There is much to be done in expanding, improving, and developing new programs of disease detection and physical restoration. It is for this reason that we wish to continue these activities with as much vigor as possible in 1962.

COMMUNITY HEALTH SERVICES FOR CARE OF THOSE WITH CHRONIC DISEASES

This brings us to our second fundamental: community health services directed to the chronically ill and the aging. This an area where we believe that even greater vigor is necessary. These are the kinds of services that can bring new life to the homebound and to the disabled who are not in need of institutional care. They are of importance to all forms of disability, whether it be heart disease, cancer, arthritis, senility, or other types of long-term disabling illness.

I think this principle can best be illustrated if I give you an actual case history. Mrs. C., a resident of Detroit, suffered a stroke with right-sided paralysis and loss of speech. She had two young children. She was hospitalized a month during the acute stage of this illness, and then was discharged to her home with a good prognosis for rehabilitation, but still in need of considerable care.

At this point, through arrangements by the physician, the local program providing home health care services was called upon. A nurse, a physical therapist, an occupational therapist, and a homemaker, all part of this home health service, soon developed a coordinated program to help this patient. The nurse assisted the patient in overcoming her fears and anxieties. The therapist worked to conserve and strengthen muscle and joint function; and the homemaker was able to motivate the patient to care for herself and gradually to take over direct responsibilities for the home and the children.

By the end of 6 months this lady was able to take care of her children and her home, although she still had some speech difficulty.

Mrs. C.'s situation had all the potentialities for a life of prolonged and near-total disability, a disrupted home, a prolonged burden on the family income. But a community health service—in this case a Visiting Nurse Association in Detroit—saved that family as it can numerous other families and individuals if community awareness of these problems is translated into community action.

BUDGET FOR 1962

Stimulating and assisting communities in developing the kind of services needed for the care of the sick at home and for providing guidance and help to older people in maintaining their health are the two objectives demanding increased emphasis. The entire increase which we mentioned as $612,400, Mr. Chairman, I think, with the new administration, now stands at $2,572,400, if I am correct. Is that right?

Mr. Ackerman. That is right.

Mr. Fogarty. You have a budget amendment of $1,960,000.

Dr. Knott. Which brings it to a total of slightly over $2.5 million.

Mr. Fogarty. Is that in the overall budget we have before us?

Mr. Kelly. It is not in the justifications, sir. It is in a separate justification which was submitted.

Dr. Knott. In any event, this entire increase which we have requested for 1962 will be directed to these objectives, namely, community health services, because this is where we feel that the major emphasis should be given.

This increase will permit the establishment of various types of demonstration community health programs in some 70 or more communities throughout the country—demonstrations which will stimulate other communities to take similar action.

The White House Conference on Aging, the recently enacted Medical Assistance Act for the Aged, and the concerns expressed by the Congress reflect increasing public awareness of the problem and are strong evidence of a public demand and public willingness to find solutions in the States and in the communities to deal with this problem.

Our part in the Public Health Service is to provide the stimulation, support, the tools, and other forms of assistance to put established knowledge to work.

STATE PLANS TO IMPROVE NURSING HOME CARE

One final aspect of community services of great importance to the chronically ill and the health of the aged is the nursing home. During 1961 the Congress made available an increase of $150,000 for direct operations and $2 million in State formula grants for the improvement of patient care in the Nation's 25,000 nursing homes. I think you have heard Dr. Shafer comment on this.

Currently 47 States have submitted plans which have now been approved covering a wide variety of activities providing for such services as professional consultation to nursing homes, the training of nursing home administrators, the improvement of inspection services, and other measures, all designed to improve the quality of care and to enhance the protection of patients.

RHODE ISLAND

Mr. Fogarty. Has Rhode Island submitted a plan?

Dr. Knott. Yes, sir, it has.

Mr. Fogarty. Will you supply it for the record.

(The information requested follows:)

Rhode Island Nursing Home Plan

A cooperative approach to the problem of raising standards of patient care in nursing homes is being developed jointly by the State department of health and the State department of social welfare.

The State department of welfare has legal responsibility for the licensure and inspection of nursing homes, convalescent homes, and homes for the aged.

The State health department has the resources to provide leadership and technical and professional assistance in fields such as nursing training, nutrition, narcotics control, pharmacology, and sanitation; and has access to assistance in building design, physical rehabilitation, and vocational rehabilitation.

Educational materials will be supplied by the health department, division of health educaton. These will include booklets, pamphlets, films, and exhibits.

The division of health education, in cooperation with the division of public health nursing, will also function as a clearinghouse for professional and technical materials such as manuals, reports or research studies, outline guides for training courses for nursing home personnel, recommended training films, and so forth.

A first step is the assignment of a State health department public health nursing consultant to the social welfare department to develop adequate standards and techniques for nursing services. This nurse will work with welfare department personnel presently assigned to the licensing program.

Other consultation will be available from the department of health in the areas of sanitation, nutrition, pharmacology, and health education.

As rapidly as possible the program will be developed in the following steps:

1. A conference of all State health department personnel to develop a consultation program and to plan seminars, workshops, conferences, and meetings for nursing home personnel.

2. A joint conference with State department of welfare personnel to coordinate program activities, to arrange for producers, clearances, exchange of information and correspondence, and to delineate areas needing policy coordination.

3. Because of the start of program activity after the middle of the fiscal year, a sum of money not allocated for salaries will be available in fiscal year 1961 to pay for educational materials, outside professional and technical consultants, workshop leaders, seminar speakers, and so forth.

4. The records available in the office of vital statistics will be analyzed to see what additional coding, sorting, and tabulating might prove fruitful in identifying problems deserving a high priority. As a final step, the coding of death certificates by name and location of institution will be reinstituted.

The philosophy of this department will be that major emphasis should be placed on education, negotiation, and persuasion to improve standards through consultation activities, but that vigorous enforcement, including publicity, if necessary, should be an essential part of the total effort. This will mean that health department activity will in no way be seen as an alternative to the licensing and inspection activities legally mandated to the State welfare department.

Dr. Knott. Three additional States have submitted plans which are now being reviewed. As Dr. Shafer has mentioned, some 157 full-time people—physicians, nurses, inspectors, and social workers—have been added to State staffs and to community staffs and 43 part-time personnel. All these are employed or to be employed according to the plans.

In addition to providing guidance and help to the States and developing these worthwhile plans, the internal activities of the division have included the development of a minimum standards guide for use of State legislatures and their licensing agencies in development and revision of laws and regulations pertaining to nursing homes.

We expect this document to come off the press in the spring of this year.

In 1962 we propose to continue the nursing home activities which we are currently finding to be most effective. These are strengthening working relationships between hospital and nursing homes; developing model record systems for nursing homes; organizing training courses for nursing home personnel in the care and rehabilitation of patients; improving nutritional services; and assisting State agencies in developing the kinds of programs that will help them to elevate the standards of care in nursing homes.

In this summary statement, Mr. Chairman, I have tried to touch upon the highlights of our activities aimed at the prevention of disability and the strengthening of community health services for the chronically ill and the aged. For these operations, the budget as amended provides $3,958,000, which represents an increase of $2,572,400 over the 1961 level.

It may be of interest to you and the committee to know that we have a substantial backlog of requests for assistance from State and local health agencies, and we will be in a position to move forward immediately if and when the additional funds are provided.

Mr. Chairman, I shall be glad to answer any questions that the committee may have about this program and the budget requests.

Mr. Fogarty. Can you prevent diabetes?

Dr. Knott. No, sir, we cannot prevent diabetes. We can detect it early and prevent some of the complications. Diabetes is one of the three major causes of blindness.

GLAUCOMA

Mr. Fogarty. How does your work in glaucoma compare with the work that is being carried on by the Institute of Neurological Diseases and Blindness?

Dr. Knott. Ours is the application program, Mr. Chairman. Our job is to go out and stimulate case-finding activities. We collaborate with the National Institute of Neurological Diseases and Blindness to see if there are some means by which we can improve the detection technique—other ways which we might find to detect glaucoma earlier.

Mr. FOGARTY. What other ways are there than going to a doctor and having your eyes examined?

Dr. KNOTT. In any case, it requires a physician to examine the eyes under the present system, using a tonometer, a small instrument placed on the surface of the eyeball after application of an eye anesthetic.

Mr. FOGARTY. The incidence of glaucoma is growing too, isn't it?

Dr. KNOTT. Yes, sir.

Mr. FOGARTY. It happens to people in middle age or before they reach the age of 60 or 65?

Dr. KNOTT. That's right.

Mr. FOGARTY. Actually it is there for some time before it is discovered, isn't it?

Dr. KNOTT. That's right.

Mr. FOGARTY. But it could be picked up if you went to a physician and were examined once a year?

Dr. KNOTT. With your permission, Mr. Chairman, I think in answer to your question I have a letter written by an assistant highway district engineer, addressed to the State health department in Connecticut in this case. With your permission I should like to read it. I think it will illustrate the point that you are making.

The letter reads as follows:

> I was one who volunteered to participate in the accident prevention study recently conducted in the Hartford area. As a result of the physical examination I was referred to my family physician, who in turn referred me to an eye specialist.
>
> The eye specialist, Dr. S., concurred in the findings of the medical screening staff and concluded that I suffered from glaucoma. The disease is in its very early stages and constitutes a borderline case, which can be effectively and successfully controlled by the use of drugs.
>
> I should like to take this opportunity to offer my sincere and heartfelt thanks to all those people who conducted this survey, as my doctor has informed me that this disease, allowed to go undetected and untreated, could result in serious damage to my eyes.
>
> Thank you again.

We don't often get letters like this, Mr. Chairman.

Mr. FOGARTY. I think that is a good example, I think more people ought to go to their eye doctor once in a while and be examined.

Dr. KNOTT. We believe that everyone over 45 who goes in for an eye examination just for refractive errors should be tested. It is a little more difficult test to perform than in the case of diabetes, because it requires placing a few drops of anesthetic material in the eye and placing an instrument—I have one here, by the way, a tonometer—on the surface. This has to be done with some skill.

Mr. FOGARTY. It doesn't take very long, does it?

Dr. KNOTT. No, sir. I recently had it done. I think it took 3 minutes.

HOME CARE

Mr. FOGARTY. In home care, I was very pleased with that example you gave, I think that we ought to be doing more in that field than we are doing. I was in England a couple of years ago. They are 10 or 15 years ahead of us, aren't they?

Dr. Knott. That's right, sir. I think the Scandinavian countries are also.

Mr. Fogarty. They have been doing a good job in home care in the Scandinavian countries. It has cut down, so they told me, the population in hospitals. Also the people like it better. They would rather stay in their own homes.

Dr. Knott. That's right, sir.

COOPERATION WITH THE OFFICE OF VOCATIONAL REHABILITATION

Mr. Fogarty. How does this example that you gave compare with the similar work that is being carried on by the Office of Vocational Rehabilitation.

Dr. Knott. The Office of Vocational Rehabilitation essentially provides the funds for those who are employable who need some corrective activity such as surgery or medical treatment in order to rehabilitate them, and funds for vocational training.

We work in close collaboration with them. Our program has a liaison person, and we are working together in our regional offices, for example, to stimulate the development of the prevention of disability as well as the correction of disability.

PERSONNEL, 1961 AND 1962

Mr. Fogarty. How many people do you have working on this home care program?

Dr. Knott. At the present time we have our regional office people, numbering about 24.

Mr. Fogarty. Do you have one in each regional office?

Dr. Knott. We have a medical officer in each regional office.

Mr. Fogarty. Is that all he does, work on the home care program?

Dr. Knott. No, sir. This is only part of it.

Mr. Fogarty. That isn't much.

Dr. Knott. No, it isn't. We would have to add additional people.

Mr. Fogarty. How many other people do you have?

Dr. Knott. In the headquarters branch—do you have that figure?

Mr. Ackerman. It is broken down by various categories. I think if you wanted home care totally, we would probably have to furnish that.

Mr. Fogarty. Will you furnish it. I don't think you are doing half enough in that area.

Mr. Ackerman. Yes, sir.

(The material requested follows:)

Chronic diseases, home care, includes the subactivities care of the sick at home, coordinated home care, and homemaker services.

In 1961, there are seven people (five professional and two clerical) involved in the home care area. These are located in the field.

In 1962, a total of 41 people will be working in this area. Six people (four professional and two clerical) will direct the care of the sick at home project at headquarters.

Thirty-five positions will be located in the field, eleven people (10 professional and 1 clerical) will work on the development of new cooperative projects in the care of the sick at home activity.

Twelve people (10 professional and 2 clerical) will develop cooperative projects connected with the coordinated home care activity.

Twelve people (nine professional and three clerical) will serve as project officers and assistants for new homemaker services cooperative projects.

Dr. KNOTT. I think we would agree, Mr. Chairman, that we are not doing enough.

Mr. FOGARTY. I think you should be doing more. Of course you can't do any more until you get some funds.

BUDGET AMENDMENT

Now will you give us a brief justification for the budget amendment of $1,960,000.

Dr. KNOTT. Yes, Mr. Chairman.

Mr. FOGARTY. You can put a more complete statement in the record and summarize it now, if you would like.

Dr. KNOTT. This entire amount, Mr. Chairman, would be directed to community services and the home health services, especially home nursing services.

Mr. FOGARTY. Am I right in saying it is $1,960,000?

Mr. ACKERMAN. That's right.

Dr. KNOTT. That is correct.

Mr. FOGARTY. You can put the breakdown in the record and then give us a brief explanation of how it is going to be used.

Dr. KNOTT. Yes, sir.

(The information requested follows:)

The need for the development of community home health service has been widely publicized and amply demonstrated. Community awareness of this need for developing new services to care for the aged and the chronically ill in their own homes is at an alltime high. The principal deterrent to new program development has been the lack of funds to provide for the initial organization and development of such services. Funds requested will be used for assisting communities to develop new services and expand existing services in the following areas:

Home nursing care (care of the sick at home), 12 positions, $660,000.
Nursing homes, 12 positions, $225,000.
Coordinated home care, four positions, $300,000.
Homemaker services, five positions, $425,000.
Periodic health appraisals, three positions, $100,000.
Central information, referral, and counseling service, six positions, $250,000.

The increase of $1,960,000 requested will be utilized to support increased staffing and cooperative projects with State and community health departments. Agreements will be written with 70 to 80 communities in different geographical areas with one-half of the support of the new programs being provided by the community. Maximum period for which Federal support will be provided would be 4 years, and such support would be provided on a gradually diminishing basis. Each separate project would serve as a demonstration to show other communities how their resources might be utilized to provide improved services to their chronically ill and aged.

Dr. KNOTT. They are all directed to community health services, with the exception of $225,000, which will go to the improvement of care in nursing homes, which is a part of community health services in a sense, except that this is institutional care rather than home care.

Mr. FOGARTY. What can you do with $225,000? You have 25,000 nursing homes, don't you?

Dr. KNOTT. That's right, sir.

Mr. FOGARTY. You are not going to be able to do much with $225,000.

Dr. KNOTT. We can add people who can work with the States, of course, to assist them in improving the care in nursing homes. This is to stimulate and put to work the money that is available for nursing home care in the general formula grants for States. They need suggestions in this program area, and we have provided them in the form of consultation and technical assitance. We continue to do this.

MOBILE TESTING UNITS

Mr. FOGARTY. On page 51 you say:

> In many States tests for various diseases have been combined. In Kansas, organized programs are conducted throughout the State utilizing portable testing equipment and volunteer community help. In Arizona, the tests are administered using a mobile unit which houses the various pieces of testing apparatus. This project, initiated 2 years ago, is being duplicated in New York State, in Oklahoma, in Connecticut, and more recently in Wisconsin.

What do you mean by this consolidation?

Dr. KNOTT. This is bringing the various detection tests together to form a battery of tests, Mr. Chairman.

Mr. FOGARTY. You mean making five or six tests at one stop?

Dr. KNOTT. That's right, sir.

Mr. FOGARTY. Give us an example of what tests you make.

Dr. KNOTT. Diabetes is one. Glaucoma is another. Hearing testing is still another. In some instances, in some clinics where it is appropriate, cervical cytology for the detection of cancer. Detection of hypertension or cardiac or heart conditions. We try to bring these all to bear in testing the individual as a whole. We don't like to go at it piecemeal. We prefer to combine as many tests as possible.

Mr. FOGARTY. Do you have portable X-ray——

Dr. KNOTT. X-ray of the chest; that's right, sir.

Mr. FOGARTY. This X-ray testing is being carried on by the States now, isn't it?

Dr. KNOTT. That's right, sir.

Another test which is frequently included, which I should have mentioned, of course, is venereal disease testing also.

Mr. FOGARTY. Do you have any problem with the local medical societies in connection with this program?

Dr. KNOTT. Yes, sir; on occasions the local medical societies object to instituting these tests. But time, patience, and persuasion sometimes win out.

Mr. FOGARTY. When something shows up, that person is referred to a doctor in that town or city anyway.

Dr. KNOTT. That's right, sir.

Mr. FOGARTY. I know up my way the district nurses always cooperate in similar tests.

Dr. KNOTT. I think in Rhode Island, Mr. Chairman, for example, much of the cervical cytology for the early detection of cancer is carried on in a number of hospitals. In some instances it is carried on by a public agency. But in any case, in these detection tests the individuals are referred to their physicians and the results are sent to the physicians. They are not given to the patient himself.

Mr. FOGARTY. When the X-ray unit comes around to the little town I live in, it is the district nurses who stimulate the people and get them to come. Many other things are picked up, aren't they, through a chest X-ray?

Dr. KNOTT. Yes. Cardiac conditions may be picked up; lung cancer, of course, as well as tuberculosis.

Mr. FOGARTY. Is the fear of too many X-rays dissipating?

Dr. KNOTT. We haven't run into that problem, sir, as far as our program is concerned.

Mr. FOGARTY. Two or three years ago there was some question about the number of X-rays a person ought to have, wasn't there?

Dr. KNOTT. Yes, there was, sir.

Mr. FOGARTY. This is something similar to a program that was carried on down in Richmond 13 or 14 years ago. Is that right?

Dr. BAUER. That's correct; and in Atlanta, Ga.—multiple screening, they called it.

Mr. FOGARTY. Multiple screening, where they would take over an entire floor. They had the cooperation of the local medical society, as I remember it.

Dr. BAUER. Yes. It depends upon the leadership of the health department, too. If he can get his medical society to go along, it works very smoothly.

Mr. FOGARTY. I thought that was a very good project at the time.

Dr. KNOTT. Mr. Chairman, I believe this might be of interest to you. Multiphasic testing—which is another name for multiple screening—has been going on in California with certain organized labor groups. Here is a report:

> Mortality over a 10-year period was 41 percent higher among longshoremen who failed to take multiphasic medical screening tests than among those who did take them.

This is a report given to us by Dr. Lester Breslow of the State department of public health. We feel that the early detection of disease can help these people and can prevent disability, illness, and premature death.

Our job is to stimulate the States to do the job. For example, in diabetes at the present time I think throughout the country we are testing about 1 percent of the population. We would like to reach the ultimate goal of testing 4 percent of the population, particularly those who are over 40, those who are obese, or those who have given birth to a series of large babies—and particularly those who have relatives with diabetes. This is an example.

But there is much to be done in stimulating and developing these programs in the States, expanding them and perfecting them.

Mr. FOGARTY. You can give several examples of Federal stimulation to the States where the States have then taken over the operation of a program in 2 or 3 years. This cytology test you have just mentioned was a 3-year program, and now the Federal Government is no longer in it. This mass X-ray for tuberculosis only lasted 2 or 3 years as a Federal program, didn't it?

Dr. KNOTT. That's right, sir. But a lot of States still continue to do it. In your community and mine we still see the X-ray unit.

COOPERATIVE AGREEMENTS

Mr. FOGARTY. On page 54, you say:

> In order to initiate a program to provide nursing care of the sick at home, cooperative agreements will be negotiated with a minimum of 6 to 8 communities * * *.

What do you mean by cooperative agreements? Agreements between communities?

Dr. KNOTT. Agreements between the Public Health Service on the one hand and States and communities on the other, in which we provide 50 percent of the cost and the community provides 50 percent of the cost, which is the way we happen to operate it.

Mr. FOGARTY. This is one way the smaller towns could take advantage of such an arrangement, isn't it?

Dr. KNOTT. This is the ideal way to set up "seeding" programs, as we speak of them in community health services. This is what we hope to use the slightly over $2.5 million increase for—cooperative agreements.

FUNCTIONS OF A PROFESSIONAL HOMEMAKER

Mr. FOGARTY. What is a "homemaker"? What is the definition of a "homemaker"?

Dr. KNOTT. A "homemaker," Mr. Chairman, is an individual trained to go into the home and carry on all the activities, the cooking, the washing, and more or less manage the home. More recently, in some communities, the homemaker also gives modified personal care to the patient under the guidance or instruction of the nurse and physician. But, generally speaking, I guess another term that would be understood is "housekeeper"—but they are more than a housekeeper, because they are trained.

Mr. FOGARTY. Do you think a married person makes a better homemaker than a single person?

Dr. KNOTT. I can't answer that, Mr. Chairman. I don't think there is much difference so long as they are properly trained.

Mr. FOGARTY. You don't?

Dr. KNOTT. No, sir.

Mr. FOGARTY. Sometimes practical experience amounts to quite a bit, doesn't it?

Dr. KNOTT. Yes, it does, sir. But I know many single people, particularly older women, who could do an excellent job.

COMMUNICABLE DISEASE ACTIVITIES

Mr. FOGARTY. For communicable disease activities, Dr. Smith, you are requesting $9,275,600, an increase of $847,000, and 86 positions. Will you supply for the record a breakdown of these positions?

Dr. SMITH. Yes, sir.

(The information requested follows:)

Breakdown of positions, Communicable Disease Center

Grade	Position	Number	Amount
GS-12	Scientist	2	$17,930
GS-11	do	11	83,281
GS-11	Statistician	1	7,571
GS-9	Scientist	3	19,344
GS-7	Nurse	1	5,366
GS-7	Scientist	9	48,294
GS-6	Laboratory technician	1	4,846
GS-5	Engineering assistant	1	4,347
GS-5	Laboratory technician	16	69,552
GS-5	Scientist	1	4,347
GS-4	Laboratory technician	11	44,616
GS-3	Clerical assistant	1	3,765
GS-3	Laboratory technician	6	22,590
GS-2	Animal caretaker	2	7,030
GS-2	Laboratory technician	3	10,545
GS-1	do	2	6,398
	Ungraded positions at hourly rates equivalent to less than $12,210: Laborers	2	5,658
	Commissioned officers:		
	Full grade	1	7,440
	Senior assistant	12	72,432
	Total new positions	86	445,352
	Deduct lapses		47,552
	Net cost		397,800

Use of Additional Funds

Viral diseases (+49 positions; +$387,200): To attempt the resolution of certain problems created by the use of live-virus polio vaccine; increase exploitation of developments related to encephalitis and hepatitis; and conduct concurrent epidemiologic and laboratory investigations during outbreaks of gastroenteritis.

Biology and control of disease vectors (+5 positions; +$60,000): Refinement of residual fumigant technique for controlling house-frequenting mosquito vectors of disease.

Staphylococcal and other institutionally acquired infections (+11 positions; +$150,000): Expanded studies to develop more accurate diagnosis and more complete reporting. Development of fluorescent antibody identification of the "epidemic strains" and the determination of the relationship between known environmental contamination and risk of exposure to virulent organisms.

Epidemic services, including surveillance of live-virus polio vaccine (+11 positions; +$165,000): Provide 10 additional Epidemic Intelligence Service officers to respond to increasing demands for services, and extended assignments to specific investigative areas with major emphasis on surveillance activities associated with the use of live-virus polio vaccine.

Diagnostic services, including laboratory development (+10 positions; +$85,000): Initiation of a continuous program of evaluation and improvement of diagnostic laboratory activities in the State public health laboratories.

GENERAL STATEMENT ON COMMUNICABLE DISEASE ACTIVITIES

Mr. Fogarty. Now give us a statement on this activity.

(The statement follows:)

Statement by Chief, Communicable Disease Center

Mr. Chairman and members of the committee, 140,000 people die of communicable diseases and their sequelae in the United States each year. One-fifth of all the young people—those under 35—who die, die of communicable diseases. Our people—and our economy—lose 319 million workdays and schooldays a year because of communicable diseases, and the days of misery these diseases cause are countless.

The ultimate mission of the Communicable Disease Center is to eradicate these diseases; and as every year brings new insight and better means, we go forward with confidence that it can some day be done. In the meantime, in the practical tradition of public health, we use what we have to prevent illness and death from communicable disease.

Last September a new Communicable Disease Center was dedicated for the purpose not only of carrying on applied research on the communicable diseases but of hastening the use of new knowledge for the benefit of all our people. Better health for the Nation requires basic research, in which new facts about man and the world are sought; applied research, in which ways to use these new facts are developed; and action to put knowledge and methods to use so that research results can truly serve the public. At all times, care must be taken to relate these three activities in order to promote rapid progress from research results to beneficial action. The program of the Communicable Disease Center is geared to minimize possible lags; our scientists are continually alert to new discoveries that may offer new means of controlling communicable disease; our publications and training activities as well as our fieldwork keep information flowing to the States.

Present possibilities in the control of communicable diseases range from recognition of a disease condition to eradication of a disease. Intestinal flu, for instance, is recognized by most people as a harassing condition that keeps them home from work and makes them miserable. In efforts to define this ambiguous illness, Communicable Disease Center scientists have recently been able to isolate many viruses from intestinal flu patients—and, curiously enough, viruses that have not in the past been associated with any illness. We must follow this clue to see whether any such virus is a disease agent and, if so, how it spreads. These steps must be taken before control measures can be developed.

Infectious hepatitis is a disease about which we know a little more—are a little further along. For one thing, it can be fairly reliably diagnosed although the procedure is laborious because we cannot yet isolate the causative virus in the laboratory nor infect animals with it. Through careful observation and investigation of hepatitis outbreaks, Communicable Disease Center epidemiologists are often able to discover the source so that further spread of disease can be prevented. Recently, for instance, an outbreak in a school was found to have occurred among children who drank from one water source, whereas none of the children who drank from another were infected. Not only must this kind of work be pursued vigorously, since hepatitis is known to occur in long-term epidemic waves, and we are now in a period of upswing toward increased occurrence, but also we must continue strenuously efforts in the laboratory to isolate the agent.

Two years ago, experts were agreed that hospital-acquired staphylococcal infections could be prevented by better housekeeping in hospitals. To the extent that this is true—and indeed improved practices have cut down infection—staphylococcal diseases could be placed among the controllable diseases. Still, the Communicable Diseases Center has responded to 58 requests in the past 6 months for help in institutional outbreaks—and these continuing outbreaks have sent our people back to the laboratory to find out how staphylococcal organisms cause disease, and to investigate the instances where the causative organism appears to be a variety which was previously considered nonpathogenic.

Encephalitis, about which this committee has heard a good deal in earlier years, can be said to be controllable in the sense that we know it is mosquito-borne. However, this information, useful as it is when an epidemic occurs, does not help much in preventing epidemics. The Communicable Disease Center is always ready, with the expertise developed in malaria control days, to help in mosquito-control campaigns in localities under threat of an encephalitis epidemic. At the same time, our people are looking for ways to prevent both the threat of epidemics and the sporadic cases that are now believed to occur. Perhaps answers will be found in better identification of mosquito vectors, or in the mysteries of where the virus lodges out of season, or in a protective vaccine. As this committee knows, several types of encephalitis occur in this country, each presenting its own special problem. Along with the headquarters laboratory, center field stations in Colorado, Washington, California, Arizona, and Massachusetts are engaged in encephalitis work. Recently, evidence that Indians in Florida have been infected with the Venezuelan encephalitis virus, never before found in this country, has presented a new and pressing problem.

In public health, as in other areas, knowledge comes in pieces that must be fitted together, and new knowledge sometimes corrects or extends old patterns. After the virus that causes rabies was identified, and a vaccine that protected animals from rabies was developed, the control of this inevitably fatal disease was considered to depend essentially upon the vaccination of dogs. Community animal vaccination campaigns have had considerable success. However, 20 people have died of rabies in this country in the past 3 years and over 30,000 people must submit each year to the sometimes dangerous Pasteur treatment after having been bitten by a dog or cat that had not been vaccinated or could not be located. Much still needs to be done just on this domestic animal control campaign; but as urgent at the present time is following through on leads indicating that bats in the Southwest, skunks in the North Central States, and foxes in the Southern States constitute reservoirs of rabies that can and do spill over to domestic animals and to man. Indeed, since rabies in bats was recognized as a problem a few years ago, five persons have died of disease attributable to bites of rabid bats. A recent development, not yet fully investigated, hints at a new lead—two scientists working in the center's field station in New Mexico have uncovered astonishing evidence that animals may be infected simply by being in caves with rabid bats, without being bitten. Because of the shortage of competent specialists, these scientists, as well as those in the Wisconsin field station and at headquarters in Atlanta, must serve not only as investigators but as consultants to the States on rabies control.

In streptococcal sore throat, a precursor of heart and kidney disease, we have an example of disease which has recently become controllable because of an important application of research knowledge. Excellent treatment has been available for some years, and now the problem of diagnosis—the need to identify the particular strains of bacteria that can cause permanent damage—has become enormously less difficult by the fluorescent antibody technique. This laboratory method, which has been reported to this committee in detail before, is now growing in use as a tool in the investigation of many diseases. While the basic principles have been well worked out further developmental work is needed to apply it for use in identifying other organisms.

Substantial increases in reported infectious syphilis in the past 3 years, and in the first quarter of the fiscal year a 73-percent increase, the sharpest rise ever reported makes us realize that the disease is not yet controlled. Over 12,000 cases of infectious syphilis were reported in 1960, an increase of 53 percent over 1959. These increases are being reported from all over the country, in all races, from private physicians as well as public clinics. This indicates that syphilis is not yet controlled.

An emergency concept in syphilis epidemiology has been adopted throughout the country, by Federal, State, and local workers. In this emergency, the venereal disease control program of the Center is redirecting its resources, both personnel and funds, to the infectious syphilis problem. The prime need is manpower for intensified contact interviewing to speed the followup of reported cases and named contacts, for field investigations and cluster testing where epidemics emerge or threaten, for personal visits to alert physicians so as to increase their level of suspicion about syphillis and enlist their cooperation with health departments.

Evidence that these measures are effective comes to us in the fact that in 1960 almost four times the proportion of private physicians' cases were interviewed as in 1954–58, and health department casefinding traced and brought to treatment some 5,900 infectious syphilis cases—half again as many as in 1959—before they had opportunity to spread their infection further.

While the Center staff has been giving first attention to the critical situation in syphilis control, the additional appropriation of the Congress last year has enabled us to contract with universities and other outside agencies for projects aimed at applying the fluorescent antibody technique to the difficult problem of diagnosing gonorrhea. When experience in field application is satisfactory, then the fluorescent antibody can become part of the armamentarium of State and local programs.

As pieces of knowledge fit together into a clearer pattern of a disease and its epidemiology, and control methods, through applied research and experience, become more effective, some diseases reach a point at which control effort can be called containment. Such a disease is tuberculosis. Once the most destructive of all diseases, tuberculosis is now being steadily pushed back toward eradication. The 60,000 new cases reported in 1959, and the 12,000 deaths, represent continuations of downward trends. Research continues to produce better methods of control, and refinements of existing methods—and has sounded no new alarms to slow our progress.

For the containment of tuberculosis, for its advance toward eradication, the single most important present need is adequate treatment of all the persons who have active disease. Chemotherapy, which Public Health Service studies over the years helped to refine as a useful tool, is now recognized as a primary public health measure heretofore not fully applied. This thought was emphatically voiced by the Arden House Conference on Tuberculosis in 1959, and since then States and communities have been showing renewed vigor and enthusiasm in their tuberculosis control efforts. A group of consultants to the Public Health Service recently set as a goal for the Nation the reduction in tuberculosis case rates from the present 33 per 100,000 population to 10 per 100,000 by 1970.

Stepping up the rate of decrease of tuberculosis case rates is going to be difficult even in the most favored States. Those with a combination of higher-than-average problems and limited financial resources need special help, and it is to these areas that the tuberculosis control program of the Center is directing its major assistance. By supplementing State and local personnel, by helping to revamp treatment and casefinding programs for greater effectiveness, by encouraging orderly attack on specific tuberculosis problems, we are not only giving direct assistance to certain areas but working out plans that can be carried to others.

The speed with which tuberculosis will be eradicated depends to some extent on our ability to prevent the disease through prophylactic treatment. As this committee knows, the Public Health Service has in progress studies on the use of isoniazid for this purpose—large-scale applied research projects which can be expected to define with some precision the practical usefulness of prophylatic isoniazid. Because of the chronicity of tuberculosis, results of prophylaxis will not have an immediate effect on the case rate, and application of the results will require effort added to present tuberculosis-control activities. Furthermore, if prophylaxis becomes the exceedingly useful tool we expect, we shall need to be able to identify specifically the persons for whom it is indicated. Our epidemiologic and laboratory studies aimed at sharpening diagnostic procedures therefore have special immediacy. We must be able to differentiate true tuberculous infection from infection atypical, unclassified mycobacteria, if prophylaxis is to hurry us on toward the eradication of tuberculosis.

Sometimes investigation into the puzzles of one disease produces byproducts that lead the way to answers for others. I should like to digress for a moment to mention such a byproduct of the tuberculosis prophylaxis studies. In an area of Alaska where these were in progress, center scientists working on intestinal parasites discovered that there was less of one form among persons who were taking isoniazid to prevent tuberculosis. Now we are pursuing this lead in Puerto Rico, where tuberculosis prophylaxis studies are also being done and where amebiasis is a serious problem.

The starts and stops, the obstacles and puzzles of disease control make one hesitate to suggest that a disease is at the eradication point until eradication is all but an accomplished fact. However, we believe that poliomyelitis is soon to be a candidate for a massive reduction program. Oral polio vaccine, made from an attenuated live virus, makes this concept possible. In addition to ease in administration, it has the theoretical advantage over Salk vaccine that it not only prevents paralytic polio in the person immunized but prevents his harboring and spreading the virus. As the population is immunized in this way, the dangerous types or wild viruses may not be able to perpetuate themselves, and, we hope, will gradually die out and leave the Nation free of paralytic poliomyelitis.

In the coming year, intensive efforts will be needed to see that the new vaccine is widely and properly used, and at the same time to find the best ways to give it. Field investigations by trained epidemiologists must determine how rapidly it produces immunity and whether it can stop epidemics. Laboratory work in the States and at the Communicable Disease Center will have to separate not only polio virus from other enteroviruses—ECHO and coxsackie—but the virulent types of polio virus from the attenuated. Continuous laboratory surveillance must keep watch on the oral vaccine virus to make sure it undergoes no changes that could make it virulent. For this work, laboratory personnel must be trained. There is much work to be done as the Nation moves toward eradication of poliomyelitis—work toward a major triumph in public health.

Not only in poliomyelitis, but in work on all the communicable diseases, from recognizing them to eradicating them, laboratory work of a high order is essential. Training provided by the Communicable Disease Center to State and local laboratory workers has increased their competence, but at the same time has brought to the Center a heavier load of difficult laboratory work and also a great demand for materials that we produce which are available from no other source. State and local laboratories are now recognizing many thorny problems that they would have missed in the past and that require special tests, which only a few State laboratories are equipped or staffed to perform. Our hope is to be able to carry this load, since we feel it represents real progress toward better health for the people of the United States.

Most of the preceding has concerned disease problems within the bounds of the old 48 States. In addition, the communicable disease activity supports activities in two areas which have distinctive problems—the Arctic and the subtropics.

Alaska contains a vast unused land resource that must be prepared for considerable population growth. To do this requires sustained and substantial research effort to acquire medical, biological, and environmental health knowledge. The Arctic Health Research Center of the Public Health Service, in Anchorage, Alaska, is the only permanent installation outside the U.S.S.R. that conducts such studies. Not only does the small permanent staff of the Arctic Health Research Center conduct studies itself, but this Center provides support, space, and services to other governmental and nongovernmental research scientists. At the present time the work of this Center is primarily concerned with the communicable diseases, which cause much greater mortality and morbidity in Alaska than they do in the older States. The important investigations of these diseases—diarrheal diseases, tuberculosis, trichinosis, measles, mumps—must be conditioned by the different type of environment. Contaminated water as a source of bacterial diarrhea remains a major problem in Alaska, and has led to investigation of methods of treating and creating small water supplies and of using lagoons in waste disposal. Increased emphasis in the coming year also must be placed on identification of the causes of the high infant mortality rate.

Just as the Arctic poses special communicable disease problems, so does the subtropical climate of Puerto Rico. In contrast to sparsely populated Alaska, Puerto Rico is crowded, making such diseases as tuberculosis, venereal diseases, diphtheria, and polio of greater consequence. Also unique to Puerto Rico is the problem of schistosomiasis. This is the only area of the United States that has this disease, which, with the decline of malaria, has become one of the leading public health problems of the world. In Puerto Rico, we conduct applied research into methods of controlling the snail, which is the vector of this disease.

Although eradication would seem to be the end point of disease control, diseases that have been eradicated cannot be forgotten as long as the organisms that cause them continue to exist in the world. Plague, endemic or murine typhus, and yellow fever have been eradicated from the United States, but they are all transmitted by insect vectors, and in these days of rapid transportation their reintroduction is a possibility that we must guard against. Plague is still present in wild rodents in our Western States, and while the typhus organism is not apparent now, it is known to be harbored by rats and other rodents. We have had no yellow fever for many years, but its vector, the Aedes aegypti mosquito, is still present in the Southeastern States. To help keep insects and rodents from bringing back such diseases, the Communicable Disease Center works with the States on demonstration projects such as the one now being conducted in Pensacola, Fla., to determine whether the yellow fever mosquito can be completely wiped out of a community. Applied research and the continued use of disease control knowledge must go on even after eradication, if victory over disease is to be maintained.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Dr. SMITH. Mr. Chairman and members of the committee, the ultimate mission of the Communicable Disease Center is to eradicate the communicable diseases that kill 140,000 people a year, cause 319 million lost work and school days annually, and countless days of misery. Last September, a new Center was dedicated to accomplish this mission. Constantly, we relate and coordinate basic research, applied research, and the use of knowledge, in order to promote rapid progress from research results to beneficial action. The Center's program is geared to minimize delay. Our scientists are continually alert to new discoveries that may offer new means of controlling communicable diseases. Our publications and training activities, as well as our fieldwork, keep information flowing to the States.

OUTLOOK FOR COMMUNICABLE DISEASE CONTROL

Present possibilities in communicable disease control range from recognition of a disease condition to eradication of a disease. "Intestinal flu," for instance, is an ambiguous illness we are seeking to define. Our scientists have been able to isolate many viruses, some of them never before associated with any illness, from intestinal flu patients. As soon as they identify the disease agent and find out how it spreads, control measures will be possible.

We know somewhat more about hepatitis, although the virus cannot, as yet, be isolated.

Mr. FOGARTY. You don't know what causes it, do you?

Dr. SMITH. We feel that it is a virus, yes, sir; but we haven't been able to isolate and characterize the virus.

CDC epidemiologists, carefully observing and investigating outbreaks, often can discover the source and prevent further spread. In conjunction with this work, laboratory investigations must be pursued vigorously since hepatitis, which occurs in long-term epidemic waves, has entered a period of upswing.

Two years ago, experts were agreed that hospital-acquired staphylococcal infections could be prevented by better hospital housekeeping, and these institutional infections were considered controllable. Improved practices have cut down infection; and yet, in the past 6 months, the Center has responded to 58 requests for help in institutional outbreaks, which have sent our scientists back to the laboratory to find out how staphylococcal organisms cause disease and to try to solve the puzzles presented when the causative organism appears to be a variety previously considered nonpathogenic.

The control of encephalitis epidemics, as this committee has heard in the past, depends on mosquito control. The Center is always ready to share its expertise acquired in malaria control work with localities under threat of encephalitis epidemics. To remove the threat of epidemics, however, and to prevent the sporadic cases now believed to occur, our people are looking for better identification of mosquito vectors, for answers to the mysteries of where the encephalitis viruses lodge out of season, and for a possible encephalitis vaccine. Recent evidence that Indians in Florida have been infected with Venezuelan encephalitis, a type never before found in this country, presents a new and pressing problem.

New knowledge in public health sometimes corrects or extends the patterns of disease control. For many years, rabies control has been focused on the vaccination of dogs, with considerable but not complete success. Now, however, we know that bats in the Southwest, skunks in the North Central States, and foxes in the Southeast are reservoirs of rabies that can and do spill over to domestic animals and man. A recent development, not yet fully investigated, suggests that animals may be infected simply by being in caves with rabid bats, without being bitten. This finding, if confirmed by our scientists at the New Mexico field station, will necessitate complete reevaluation of the rabies control program.

The successful application of research knowledge has placed streptococcal sore throat, a precursor of heart and kidney disease, among the controllable diseases. Using the fluorescent antibody technique to identify the damaging bacteria, the excellent treatment available for some years can be given promptly. While the basic principles of the fluorescent antibody technique have been well worked out, further developmental work must continue in order to put it to use for identification of other organisms.

VENEREAL DISEASES

Recent substantial increases in reported infectious syphilis make us realize that this disease is not yet controlled. With the sharpest rise ever reported coming in the first quarter of this fiscal year, the venereal disease control program is concentrating its resources on infectious syphilis. The prime need is manpower to speed the followup of reported cases and named contacts, to interview and reinterview for contacts and suspects, to apply cluster testing where epidemics emerge or threaten, to alert physicians in private practice, and to enlist their cooperation with the health department. Evidence of these measures' effectiveness comes to us in the greatly increased proportion of private physicians cases interviewed and in the large number of infectious syphilis cases brought to treatment before they had opportunity to spread their infection further.

At the same time, through the additional appropriation of the Congress last year, we have been able to develop field projects in the application of the fluorescent antibody technique to the difficult problem of diagnosing gonorrhea.

As knowledge of a disease and its epidemiology grows into clearer patterns, and methods become more effective, disease control reaches a point that can be called containment. Tuberculosis, once the most destructive of all diseases, has now reached this point. The 60,000 new cases reported last year, and the 12,000 deaths, represent continuations of downward trends.

TUBERCULOSIS

For the containment of tuberculosis, for its advance toward final control, the single most important present need is adequate treatment of all active cases. Chemotherapy is now recognized as a primary public health measure. Using this tool completely is difficult even in the most favored States. To those States with higher than average problems, the tuberculosis control program is giving special direct assistance by supplementing State and local personnel, helping revamp treatment and casefinding programs for greater effectiveness, and encouraging orderly attack on specific problems.

As this committee knows, the Public Health Service has in progress large-scale studies on the prophylactic use of isoniazid to prevent tuberculosis—applied research which may within a few years result in an enormously faster decline in the number of tuberculosis cases. If prophylaxis becomes the exceedingly useful tool we expect, it will not replace but be added to present tuberculosis control activities. Furthermore, we shall urgently need the knowledge being uncovered in our studies aimed at differentiating true tuberculous infection from infection with atypical, unclassified mycobacteria.

POLIO

The obstacles and puzzles of disease control make one hesitate to suggest that any disease of magnitude can be reduced to such an extent that it is no longer a public health problem. However, the use of the oral poliomyelitis vaccine which not only protects the person from paralysis but also prevents his spreading dangerous polio viruses, encourages the belief that polio soon will become a candidate for such a program.

The Center's work on polio in the coming year will include preparatory efforts to assure that the vaccine will be effectively used, as well as field investigations on its effects. Laboratory work in the States and at the Center will be needed to differentiate the various polio and related viruses and, of prime importance, to differentiate the vaccine virus from wild virulent viruses.

Not only in poliomyelitis, but in all communicable diseases, laboratory work of a high order is essential. Training of State and local laboratory workers has increased their competence, but at the same time has brought to the Center a heavier load of difficult reference specimens as well as a greater demand for materials that we produce.

The problem of communicable disease control varies from area to area, and from population to population. The communicable disease activity supports the work of the Arctic Health Research Center at Anchorage, Alaska. At this Center, research is conducted in the control of communicable diseases such as tuberculosis, diarrheal diseases, and the causes of infant mortality that are modified by the cold temperatures, as well as environmental health problems such as water supply and sewage disposal.

Activities are also supported in Puerto Rico, where applied research is conducted and control techniques developed for such diseases as schistosomiasis—now a leading public health problem in the world.

In summary, this request supports a broad program of applied research and development followed by cooperative action with the health departments of this country to promote and demonstrate rapid progress from research results to beneficial action.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

HEPATITIS

Mr. Fogarty. I see more in the papers this year than ever about the incidence of hepatitis.

Dr. Smith. Yes, sir.

Mr. Fogarty. They had an outbreak down in Mississippi, didn't they?

Dr. Smith. This is entirely true, Mr. Fogarty. The disease has always occurred in cyclical progression over 8- to 10-year spans. We have constantly, for the last 3 or 4 years, been having an increase in this particular disease. The Pascagoula epidemic was associated with oysters for the first time reported in this country.

Mr. FOGARTY. It takes quite a while to get over it; doesn't it?

Dr. SMITH. Yes, sir. It is a very debilitating disease, and it can have serious permanent sequelae.

Mr. MICHEL. My brother-in-law is just now recovering from hepatitis, which they say he got in Chicago from oysters.

Dr. SMITH. Raw oysters?

Mr. MICHEL. Yes.

Dr. SMITH. We have not traced any of the Pascagoula oysters to Chicago. I would believe that these oysters probably were not contaminated.

Mr. FOGARTY. You do say that the outbreak in Mississippi was caused by raw oysters in that area?

Dr. SMITH. Yes, sir. This was a very limited bed of oysters that was apparently contaminated. The use of these oysters was limited to the area and to the adjacent States.

Mr. FOGARTY. It could happen in other contaminated areas, though?

Dr. SMITH. Yes, sir.

FLUORESCENT ANTIBODY DIAGNOSTIC TECHNIQUE

Mr. FOGARTY. This committee was very interested in your fluorescent antibody technique several years ago and we have since felt that you haven't been doing enough in the further development of it. But you are concentrating in the area of gonorrhea, which is difficult to diagnose. Is that what you said?

Dr. SMITH. Yes, sir.

Mr. FOGARTY. Is it being used now?

Dr. SMITH. It is being used along with routine methods in several of the States and large cities on an experimental basis to popularize the method. It is being used in other areas when they have mass tests to do.

I didn't mean to leave the impression, Mr. Fogarty, that we were concentrating our fluorescent antibody development in this area.

Mr. FOGARTY. I didn't mean that, either. You meant to give that as one example of what you were doing as far as research is concerned. Are you satisfied with the amount of time you are spending on further research in this area?

Dr. SMITH. We have done two things to speed this up, Mr. Fogarty. We are keeping our methodology unit that does nothing but investigate and develop the fluorescent antibody technique as applied to different disease agents going. We have also put the fluorescent antibody test out into the specialty laboratories, and they use it not only to develop tests that will be applicable in States in disease control programs and disease diagnosis, but they also use it as a research tool, which increases the speed with which they can do other research.

Mr. FOGARTY. Just give me for the record an example of how it takes hours to diagnose with this technique as compared with days with the regular way.

Dr. SMITH. Yes, sir. Many of these can be done in a few hours.

Mr. FOGARTY. Give us a couple of examples.

Dr. **Smith.** I think the streptococcus activity is probably as good a one as any because it is being used all across the United States. This decreases from a minimum of 3 days to much less than 1. It gives the patient the diagnosis just that much faster so he can start on curative treatment.

Mr. **Fogarty.** I thought I had heard of better ones than that. What about rabies?

Dr. **Smith.** Rabies is an extremely good example. As you know, this used to have to be put through mice for the definitive test, after finding the negri bodies in the brain. Now with the fluorescent antibody test, by examination of the brain tissue, a final diagnosis is possible without carrying it to animal studies.

RABIES

Mr. **Fogarty.** Have you gotten rid of the rabies problem down in Georgia? When Mr. Lanham was on this committee, that was one thing he was always interested in.

Dr. **Smith.** We have a field station in Atlanta on rabies, working closely with Georgia. The incidence of rabies in Georgia in dogs and foxes is decreasing, but we haven't eliminated it as a public health problem from the State.

Mr. **Fogarty.** Didn't you have one in Texas last year?

Dr. **Smith.** California was larger.

Mr. **Fogarty.** California?

Dr. **Smith.** Yes, sir; and it included the borders of Texas. There were rabies epidemics in dogs and wild animals all along the United States and the Mexican border.

Mr. **Fogarty.** It is still quite a problem, isn't it?

Dr. **Smith.** Yes, sir. It is a serious problem, particularly in wildlife and in animals. The most pressing problem as we see it at the moment is the fact that in one of the caves in the Southwest we placed different kinds of animals in cages in there. With no apparent bite, some of these animals became infected with rabies.

This raises the general question of whether or not rabies is ever carried as an aerosol or as an inhalation disease. If it is, of course, this will change control techniques throughout the country. We are now recommending that all of the people who, as a hobby or as a part of their work, go into caves get prophylactic immunization. This is a problem we are working on and we surely haven't got the final answer yet.

DIARRHEAL DISEASES

Mr. **Fogarty.** What about diarrheal diseases? Have you made any headway on those?

Dr. **Smith.** We have made much headway in the general area of diarrheal diseases. The area that has been resistant to our efforts is in the viral gastroenteritis area. At the present time there are no ways to characterize viruses that will give diarrheal dysentery. Since the stools are heavily infected with many different kinds of viruses, it is extremely difficult to sort out that one that may be the etiologic agent in any specific outbreak. This we are working on actively in our Phoenix field station, where the incidence of diarrheal disease is extremely heavy.

We hope to have some answers on it at a later date.

MOSQUITO CONTROL

Mr. Fogarty. On page 63 you speak of a finding that could revolutionize methods of control of house-frequenting mosquitos.

Dr. Smith. Yes, sir.

Mr. Fogarty. What is this all about?

Dr. Smith. In any control activity that requires reduction or elimination of a house-frequenting mosquito, it has always been the custom and the accepted control procedure to spray the walls of the house and the environs of the habitation.

Last year—early last year—the scientists in Savannah came up with an insecticide that is embedded in a wax vehicle. This looks very much like a candle that is enclosed in a perforated screen. This is formulated so that the insecticide evaporates at a predetermined rate, enough to kill the mosquito without harming the occupant of the house.

This of course is much more satisfactory in the areas that we are interested in. It depends not at all on the quality or material of the wall. We have high hopes that this would be added to the control of malaria.

Mr. Fogarty. Some of these mosquitoes build up resistance, don't they, to some of these insecticides?

Dr. Smith. That is true, yes, sir; and the insecticide has to be changed back and forth, taking this into consideration.

SUPPORT OF DIAGNOSTIC SERVICES

Mr. Fogarty. In connection with your increase for diagnostic services you say on page 69 that you will give States financial support through contracts. Is this something new?

Dr. Smith. No, sir. This has been done previously. We are not thinking of this as substantial contracts to State laboratories, but as a low-level support that will allow them to enter into the training program without holding back their own routine work.

Mr. Fogarty. How much money is involved?

Dr. Smith. It is quite small. May I submit that, please.

(Dr. Smith submitted the following:)

Of the budget increase of $85,000 for diagnostic services, $15,000 will be used to provide contractual financial support to State public health laboratories.

Mr. Fogarty. Is this a one-time operation where the State will take over after this one appropriation?

Dr. Smith. This has been our experience.

VENERAL DISEASE CONTROL

Mr. Fogarty. For venereal disease control there is no increase at all, even though the incidence is going up. Did you ask the Department for more money?

Dr. Smith. May I limit this to our particular request. We requested an increase of $1.7 million to the Bureau. The Bureau allowed $1.2 million, and then later in the budget process no increase was allowed at this time.

Mr. Fogerty. So the Bureau cut you $500,000? Is that the Public Health Service?

Dr. SMITH. It did not get beyond the Public Health Service.

Mr. ACKERMAN. The estimates to the Department were $2,650,000, the Surgeon General's estimate. The Department allowed $2,650,000. I am talking about VD grants. The Bureau of the Budget allowance was $2,400,000. This is exclusive of direct operations.

Mr. FOGARTY. Do you have a vaccine for syphilis?

Dr. SMITH. No, sir.

Mr. FOGARTY. Or gonorrhea?

Dr. SMITH. We have a clue on gonorrhea that I hate to talk about at this time, since it may fall out within the next few months.

TUBERCULOSIS CONTROL

Mr. FOGARTY. What about tuberculosis? There is no increase in funds, but you are asking for 10 more positions.

Dr. SMITH. Yes, sir.

Mr. FOGARTY. How are you shifting this program to make that possible?

Dr. SMITH. The money for the prophylactic studies which have been going on and are slowly being completed is going to be diverted into assistance to States—those States which have a particular tuberculosis problem. One of the things that these States need is the assignment of personnel.

USE OF BCG

Mr. FOGARTY. In the justifications you don't mention BCG this year at all. Have you given that up?

Dr. SMITH. I think it is the considered opinion in this country that although BCG is an efficient immunizing agent it probably would hold up the progress of the control program more than it would help.

Mr. FOGARTY. You think that?

Dr. SMITH. Yes, sir.

Mr. FOGARTY. Do you disagree with the testimony we had last year from two or three doctors? Did you read that testimony?

Dr. SMITH. Yes, sir. I would like to say that in areas where the risk of acquiring tuberculosis is more significant than it is in the United States, this is still a good immunizing agent and control technique.

Mr. FOGARTY. We were told that it was outstanding in this field.

Dr. SMITH. It has one marked disadvantage in control procedures, and that is, of course, that it gives you a positive tuberculin test which eliminates one of the techniques of tuberculosis control that is extremely helpful.

TUBERCULIN TEST

Mr. FOGARTY. What about tuberculin testing of schoolchildren? Is that successful?

Dr. SMITH. Yes, sir.

Mr. FOGARTY. Does it stand up pretty well?

Dr. SMITH. It stands up very well. As to techniques that give one a real feeling of confidence, the tuberculin test in this whole field is going along very well. In some areas the typical organisms give false positives, but this is being eliminated by careful measurement and careful adjustment of the tuberculin used. It is known in this country that the tuberculin-positive citizens are much more likely to get active tuberculosis later in life than those who are not now infected. This allows you to sort them out and follow those that are a particular risk.

Mr. Fogarty. Is it being done in most school districts?

Dr. Smith. I believe it is increasing all the time, Mr. Fogarty.

Mr. Fogarty. It doesn't take very long.

Dr. Smith. No, sir; it is a simple test. It has to be given and read skillully. But it is not difficult.

OTHER VACCINES

Mr. Fogarty. What other vaccines are you working on that show promise?

Dr. Smith. We are working on one of the organisms that causes diarrhea dysentery, the so-called *E. coli.* This is ready for human testing and it seems to promise in this particular type of diarrhea and dysentery a new immunizing agent.

We are working, but haven't got to the point of testing yet, on an encephalitis vaccine. I think those are the new ones.

LOCATION OF FACILITIES

Mr. Fogarty. Where are your headquarters? Are they still in Atlanta, or are they in Washington?

Dr. Smith. Our headquarters are at Atlanta.

Mr. Fogarty. How much of your time is spent there?

Dr. Smith. I spend the great majority of my time there.

Mr. Fogarty. Is the new building big enough?

Dr. Smith. No, sir; it isn't, unfortunately. It has been working out very well for the activities we have been able to get into it, but we have had to maintain Chamblee and we have several other activities that would benefit by closer coordination and cross-fertilization, if you will.

Mr. Fogarty. Is Chamblee fireproof now?

Dr. Smith. It is no closer to that than when you saw it.

Mr. Fogarty. I would hate to be working in that place. You have a good cafeteria now, though, haven't you?

Dr. Smith. We have an excellent cafeteria.

ARCTIC HEALTH RESEARCH CENTER

Mr. Fogarty. Are you asking for any increase for the Arctic Health Research Center?

Dr. Smith. No, sir. The Arctic Health Research Center request is exactly the same.

Mr. Fogarty. Do you have any building funds in the budget?

Dr. Smith. We have with us today, Mr. Fogarty, Dr. Colyar, who is in charge of the Arctic Health Research Center.

Mr. Fogarty. Dr. Colyar may answer that, then.

Dr. Colyar. What was the question, sir?

Mr. Fogarty. I thought you were looking for a new building.

Dr. Colyar. We have asked for one.

Mr. Fogarty. What happened?

Dr. Colyar. Nothing yet.

Mr. Fogarty. Are you hopeful you may get one some day?

Dr. Colyar. We are still hopeful.

Mr. Fogarty. Or are you getting a pretty cold reception?

Dr. Colyar. I would say in our Service it has gotten a good reception.

Mr. Fogarty. It seems to me I have been hearing that for about 10 years.

Dr. Colyar. That's right. The first request was made in 1949.

Mr. Fogarty. You are not making much progress, then, are you?

Dr. Colyar. Not toward a new building; no, sir.

Mr. Fogarty. Are you making any progress in the research center on some of your major problems?

Dr. Colyar. I think in our research work we are doing well.

Mr. Fogarty. Out of your research, have you developed anything that will help to overcome some of the problems you have had in sewage disposal?

Dr. Colyar. I think in sewage we have demonstrated that some conventional methods of disposal will work in the Arctic, with certain modifications. For example, the so-called sewage lagoon or oxidation pond will work at, say, parallel 65 or 66, which is the area of the Arctic Circle. We have one which is just finishing its third winter of operation, serving a school of about 200 enrollment and 3 teacher families.

This is an open pond into which is flushed the effluent from kitchen and bathroom wastes. It takes care of itself by natural biological methods.

Mr. Fogarty. That can be done almost anywhere, can't it?

Dr. Colyar. I guess it can.

Mr. Fogarty. It is being done in many other States, isn't it?

Dr. Colyar. It is being done widely in this country.

Dr. Smith. I think the surprise is that it does work there.

Mr. Fogarty. What is your really big problem now?

Dr. Colyar. I think in the environment field our big problem is with water supplies and with sewage disposal methods. I think, say, in the next 10 or 25 years our real problem is to devise methods which are suitable to individual households and to small institutions such as schools or hospitals, and possibly small villages.

I think that we with others did design a system that will work for distribution of water in a city, and this is now operated in Fairbanks. This system will work, will prevent freezing in a municipal water distribution system. But we don't have any good methods for storage of water, for example, for household use.

When you think that for 8 or 10 months of the year most water is solid—ice—so that individual households have no source of water except for shallow supplies or deep ground water wherever it can be obtained, or by melting of ice and snow—we feel that we need to devise a storage device that would provide, say, 15,000 to 20,000 gallons of water which would be the minimum for an average-sized family for a period of about 100 to 120 days, so that they can enjoy the conveniences of running water as the rest of us do.

We feel that this would do a lot to encourage settlement.

Mr. FOGARTY. Do you have the tuberculosis problem with the Eskimoes under control?

Dr. COLYAR. I think it has been reduced to a level where a maintenance program can keep it under control.

Mr. FOGARTY. Is it still proportionately higher than other areas of the Nation?

Dr. COLYAR. It is much higher than the Southern States. I believe that the mortality rate is around 40, as against 8 or 9 for the Southern States.

Mr. FOGARTY. Infant mortality has been a big problem in this population, too?

Dr. COLYAR. Infant mortality runs around 80, which is, say, four times higher than in these States—most of these States. In some parts of Alaska, in one area particularly, where we now have a project on this, the infant mortality rate is 150.

Mr. FOGARTY. What kind of a place is that?

Dr. COLYAR. This is in Western Alaska in what we call the Bethel Area, an area of some 30,000 or 40,000 square miles with about 10,000 Eskimoes living there. It is on the lower Kuskokwim River. We are attempting to find out what specifically are the causes and what are the circumstances surrounding the deaths, as to whether or not they had available medical care; or, if not, what were the reasons.

Mr. FOGARTY. Is it a remote place?

Dr. COLYAR. No, I wouldn't say so, by plane. There is good plane travel.

Mr. FOGARTY. Is this the only research center of its kind outside of the Soviet Union?

Dr. COLYAR. To my knowledge this is the only one that devotes itself to so-called health research in cold areas.

COMMUNITY HEALTH PRACTICE AND RESEARCH

SCHISTOSOMIASIS

Mr. FOGARTY. Next is "Community health practice and research." We have talked about schistosomiasis. They told me that in the northeastern section of Brazil that is one of the leading causes of death. Is that right?

Dr. SMITH. Yes, sir. And in Puerto Rico about a fifth of the population has schistosomiasis.

Mr. FOGARTY. We have progressed to the point where there is a good prospect of getting the problem in Puerto Rico under control. That is what Dr. Ferguson told me when I was down there a few months ago.

Dr. SMITH. We are surely working on it in several different ways. The incidence is still, although decreasing, about 1 in 5.

Mr. FOGARTY. Has Brazil called upon you for any help?

Dr. SMITH. No, sir. They are following the work that we are doing in Puerto Rico, but none of our people from there have been asked or have given any consultation. On the other hand, we have worked with them on skin-test antigens from Atlanta.

PROPOSED INCREASE, 1962

Mr. **Fogarty**. You don't have an increase in "Community health practice and research," Doctor?

Dr. **Shafer**. There was only an increase of about $9,000 to annualize positions that were allowed last year for our training unit.

HEALTH PROBLEMS OF MIGRANT FARM WORKERS

Mr. **Fogarty**. What are you doing in the area of migrant farmworkers?

Dr. **Shafer**. We have a unit consisting of about three people budgeted at $25,000 per year that works on the problems in the migrant labor group. It has been in existence about 7 years. We feel that this unit has done some very fine work.

Mr. **Fogarty**. Where is it?

Dr. **Shafer**. We have a unit of three people in our office here in headquarters.

Mr. **Fogarty**. That isn't much. They might be doing some fine work, but you are not accomplishing much with three people.

Dr. **Shafer**. We have simply identified a lot of problems that we have not been able to attack because of lack of budget and staff.

Mr. **Fogarty**. You just can't do much with three people.

Dr. **Shafer**. We agree.

Mr. **Fogarty**. What have you found out?

Dr. **Shafer**. We have identified the migrant population. We know what part of the country they come from; we know the counties through which they move during the agricultural season; we have identified the diseases that are a special problem to them.

Mr. **Fogarty**. What are some of those?

Dr. **Shafer**. These people come from really depressed areas for the most part, with poor health conditions, so that they have increased venereal disease rates, increased tuberculosis, and a high incidence of gastrointestinal infections. The children and the adults lack immunization. In general terms, they have very little knowledge concerning health practices.

Mr. **Fogarty**. In general they have very little of everything.

Dr. **Shafer**. That is certainly true, Mr. Chairman. They tend to travel in substandard transportation. Their housing for the most part is not adequate.

Mr. **Fogarty**. Some don't get enough to eat?

Dr. **Shafer**. Nutrition is definitely poor.

Mr. **Fogarty**. Isn't nutrition one of the leading causes——

Dr. **Shafer**. Nutrition is a very serious problem. Just the actual storage of food in their housing is completely inadequate because they very infrequently have refrigeration for their food. So they constantly lose food through spoilage and become ill because of eating unrefrigerated food.

Mr. **Fogarty**. What have you done about it?

Dr. **Shafer**. We feel that we have the problems identified, and with staff and money we can attack these problems now.

Mr. **Fogarty**. Do you have any plans?

Dr. **Shafer**. We have plans if there were funds. We would put staff in the field, match it with staff from State and local health departments; we would actually put additional nurses and sanitarians in the field to work with the migrants.

Mr. Fogarty. What would you like to have to start off the first year?

Dr. Shafer. We had requested an additional $250,000 for this activity for our own operations. We feel that much more could be used because we have State and local health departments that are ready to go to work on this problem.

Mr. Fogarty. Put in the record how you would use that $250,000.

(The information requested follows:)

With an additional $250,000 we would:

1. Employ professional personnel and loan them to States and communities with major migrant health problems to provide health services and improve sanitary conditions for migrant workers and their families.
2. Increase our staff of consultants to work with States in developing and establishing interstate agreements and working relationships which would assure a continuity of health services as the migrant moves from one State to another.
3. Provide health education materials and instruction to the migrant families, crew leaders, and other groups who work with the migrants.
4. Establish pilot projects in cooperation with States to develop and demonstrate new methods of providing health services to the migrants.
5. Provide training courses to improve the skills of public health personnel in giving health services to migrants.

The activities would be concentrated in the States comprising the three major migrant streams:

East Coast States from Florida to New England
Midwest States from Texas to Minnesota and Michigan
Far West States from the Rio Grande border to Idaho and Washington

Mr. Fogarty. How much support could you use for the local and State health departments?

Dr. Shafer. I think a very conservative figure has been worked out on this. We could use an additional $2.5 million for additional staff and resources at the State and local level.

Mr. Fogarty. About how many positions would that amount to?

Dr. Shafer. That would undoubtedly add at least 200 positions. I would prefer to put that in the record, Mr. Chairman. I don't have it accurately in mind.

(The material referred to follows:)

This would make it possible for States and communities to add approximately 300 man-years of health service personnel to work on migrant health problems. These funds would also help provide equipment, supplies and travel expenses.

Mr. Fogarty. But you think it is important enough to do something about?

Dr. Shafer. I certainly do. I think anyone who has investigated these camps and noted the people and the conditions——

Mr. Fogarty. They don't have many to speak up for them. That is their problem. Some of the church groups are doing it now. One church group writes to me quite frequently, the National Council of the Churches of Christ. They have people up my way who are very much interested in this program.

Dr. Shafer. I think that anyone who works with the problem and becomes interested realizes the enormity of the problem. For example, we know a professor of pediatrics at Stanford who spent 3 months studying the California conditions and was so convinced that this was a major problem that he is now working full time with the California State Health Department on the migrant labor problems.

LETTER FROM NATIONAL COUNCIL OF CHURCHES OF CHRIST

Mr. FOGARTY. Here is a letter I received, dated December 24:

DEAR CONGRESSMAN FOGARTY: Knowing your interest in the health problems of domestic migrant agricultural workers, I appreciate the opportunity to bring to your attention some current developments in this area which point to a need for national leadership and action in cooperation with the States and local communities. As a staff member of the migrant ministry of the National Council of Churches of Christ during the past two decades it has been my privilege to work directly with the migrants and their families in the Atlantic Seaboard States from Florida to New England. This experience has led to a growing concern for the still unmet health needs of this large labor force due to the paucity of health facilities and services available to them. Reports of studies of this problem in numerous sections of the country confirm my observations and indicate that the exclusion of this group of our citizens (approximately a million) from normal health services is general the country over. Low income status and inability to meet residence requirements are obvious barriers to the migrant workers' use of health and medical services, but beyond this, and of immediate concern, is the sheer physical inaccessibility of such services to people whose way of life is determined by the mobility and remoteness from centers of population inherent in seasonal farm employment.

There is need, then, to work out methods and procedures—perhaps new or unfamiliar—of making available to migrant people the health services that are extended to other segments of the population as a matter of course. Would it be feasible to provide mobile clinics? Decentralized medical and dental facilities? Afterwork consultation hours? Scheduled nurse visitations? Coordination of private and public services? These and other possible approaches should be explored in depth with sufficient financial resources and technical personnel in a number of areas where migrants serve.

In view of the interstate character of the farmworker migration, we face here a national responsibility and yet the actual services must be rendered at scattered local sites. The situation obviously calls for Federal and State cooperation if improvement in the migrant health situation is to be attained.

That is just what you have been recommending.

Dr. SHAFER. I would certainly agree.

Mr. FOGARTY. The letter continues:

As you are aware, there is widespread concern about this matter in the States, as evidenced by the resolution unanimously voted by the Association of State and Territorial Health Officers at its recent meeting (October 1960) recommending that the U.S. Public Health Service reappraise the priority assigned to the health problems—including problems incident to the provision of medical care—arising from the presence of domestic agricultural migrants in both home-base and work areas, and seek additional funds and authority to provide technical and financial assistance to the States, including project grants.

I wish, therefore, to urge that the subcommittee of the Appropriations Committee, dealing with matters of public health, under your chairmanship, give vigorous support to an appropriation adequate to carry out the intent of this recommendation of the Association of State and Territorial Public Health Officers. Those of us who are in direct and daily touch with the migrant health problem feel that action in this matter is past due and that no time should be lost in implementing such a program for safeguarding the health and safety of our domestic migrant farmworkers whose labor is essential to our agricultural economy. Upon them is imposed, by the nature of their employment, more numerous and drastic health hazards than fall to the lot of the generality of our citizens.

Sincerely yours,

MARGARET H. EKSTROM,
Mrs. C. Emanuel Ekstrom,
Director, Migrant Ministry, Northeastern Area.

I believe, as these people believe, that it is past due, and something should be done. Are you familiar with the resolution adopted by the State and Territorial Health Officers' Association.

Dr. Shafer. Yes, I am, Mr. Chairman. I think it expresses the opinion that States, with a problem in the migrant labor field, are ready to go to work on it.

Mr. Fogarty. We also have a letter from them.

We have to come back at 1:30, so we shall stop now.

AFTERNOON SESSION

HEALTH PROBLEMS IN METROPOLITAN AREAS

Mr. Fogarty. The committee will come to order.

I have two questions, one on health problems in metropolitan areas and one on health problems in rural areas.

Do you want to say something about each?

Dr. Shafer. We do have the staff working on health problems in metropolitan areas. We have one person assigned to each of three large cities—Boston, Pittsburgh, and New York City. These men are working, in the case of Boston, as the city health officer; in Pittsburgh, as district health officer; and in New York City, as a research assistant.

Mr. Fogarty. What are they there for?

Dr. Shafer. They are there to provide assistance to these cities, but their principal mission is to study problems of health departments in metropolitan areas and to determine new projects that should be carried out in these cities to meet some of the special problems that exist in metropolitan areas.

Mr. Fogarty. Well if the State unit asks for some help with organizing their health services, would someone come out from your office to help find out what their needs are.

Dr. Cannon, the new health officer is known to most all of you and he wants to get started right and has asked for some assistance.

Dr. Shafer. At the present time we have a staff from our regional office in New York City helping Dr. Cannon in working out a new legislative program to bring his health laws up to date. He then hopes to move on next year to really revitalize his whole health department operation.

Mr. Fogarty. I have often thought, with our State being so small, it ought to have the best health unit in the country.

Dr. Shafer. I think they have made a real step in that direction. Their current plans, you know, call for providing all services from the State health department.

Mr. Fogarty. They raised the pay of the directors also.

Go right ahead.

Dr. Shafer. With this small start in metropolitan health problems we are getting on with working with these cities to work out new ways and means of providing health services in metropolitan areas.

As an example, in Pittsburgh, the health department is providing followup services to patients treated by local physicians in one health district in which our man is working, so as to get complete coordination of the services provided by the private physicians and the health departments.

We think this offers real promise in extending services of the health department to private physicians' patients who need followup from the health department itself.

Mr. FOGARTY. It is not a very dramatic example, though, is it?

Dr. SHAFER. It is dramatic in that it cuts down on the number of times that patients must come back to busy physicians for minor followup problems that can be handled by the nursing staff of the health department.

Mr. FOGARTY. I see.

Dr. SHAFER. And gives these physicians a chance to better handle their patient load.

HEALTH SERVICES IN RURAL AREAS

Mr. FOGARTY. What are you doing in rural areas?

Dr. SHAFER. In the rural health area, we are currently winding up our research project that was carried out in Kit Carson County, Colo.

The monograph being developed from this study is now in the editor's hands and will be printed very shortly.

As far as the State of Colorado is concerned, they are moving ahead with a project to capitalize on our findings by putting in three of their rural counties, without health services, a health worker who will be under the supervision of their director of local health services. This health worker will be the only health resource within the county and will serve to help the population meet their health problems, direct them to health services that are now existent in the State health department, and serve in much the same way as the county agent serves in the agricultural program.

This project is developed by the State and they are asking a foundation for funds to support it during the coming year.

This same study also gave us very definite information as to how health problems develop and are met in rural counties across the country, and we are now working in Oklahoma, Kansas, and South Dakota in meeting their rural health problems with findings we have had from our Colorado project.

BUDGET FOR RESEARCH IN PUBLIC HEALTH PRACTICES

Mr. FOGARTY. On page 87 you say in connection with research and development in public health practices that there is a dearth of specific research in this field. And then the budget calls for a reduction of $400. How does that go together? It doesn't make much sense to me.

Dr. SHAFER. This is the unit within our division that would be doing work in metropolitan areas and although a budget request was sent through——

Mr. FOGARTY. It shows a decrease of $400, doesn't it?

Dr. SHAFER. That is true. That is to account for the 1 less day in this next year as compared with the past year so it is essentially the same budget. But we had submitted requests for an increase in this particular item to permit us to put more people on the metropolitan situation and this was denied.

Mr. Fogarty. How much?

Dr. Shafer. $200,000.

Mr. Fogarty. For the record tell us what you would do with that $200,000.

Dr. Shafer. All right.

(The information requested follows:)

With an additional $200,000 for metropolitan health services we would—

1. Develop a pattern for securing more effective integration of health services in a State or metropolitan area where such services are now provided on an uncoordinated basis by a number of separate governmental jurisdictions. This would involve the development of necessary legislation, to effect such an integration of organizational and financing arrangements between governmental areas, of cooperative working agreements between State and local governmental jurisdictions, and of mutually satisfactory decisions on health programs to be provided.

We would contemplate conducting such an operation in cooperation with a State such as Rhode Island or New Jersey, which has major metropolitan health problems and which has a demonstrated interest in solving these problems. The estimated cost for 1962 would be $100,000 for a cooperative project or contract with one State and includes six new positions.

2. Conduct a study to identify the gaps in health services in large cities which have resulted from the changing population composition of such cities and to determine what services need to be initiated or expanded to meet these needs. Many large cities have recently experienced and continue to experience substantial changes in such characteristics of their population as age composition, economic status, educational level, and occupation. These are population characteristics which are likely to be reflected in the nature and extent of health problems and in the choice of most effective means for providing and promoting the use of health services.

We would propose to undertake a cooperative study in a large city to determine what changes in public health programs and in methods of providing health services are needed to meet these changing needs. The estimated cost of initiating such a project in one city in 1962 would be $75,000, including funds for seven new positions.

3. Establish a small headquarters unit to direct the activities of the program, to establish and maintain working relationships with other groups and organizations interested in this field, and to collect and make available national intelligence on metropolitan health problems and activities. The estimated cost of this activity for 1962 would be $25,000 and three new positions.

EFFECT OF REORGANIZATION ON DENTAL SERVICES

Mr. Fogarty. The next is Dental Services.

Dr. Bauer. Mr. Chairman, Doctor Galagan will represent the Dental Services and Resources.

Mr. Fogarty. This consolidation was one of the recommendations of the committee last year, although we didn't recommend that it be just one activity under some appropriation like this. What has been done here?

Dr. Bauer. The recommendation, as you made it, Mr. Chairman, was that we identify dental public health, and resources out of the National Institutes of Health budget and then at the time of the study session—I mean the study of the reorganization of the Public Health Service, it was recommended that the dental resources from the Bureau of Medical Services and the public health dental program of the Bureau of State Services be consolidated into one division and put into the area of community health in order that they could work with the other programs in delivery of services to the people.

Mr. Fogarty. Was this a little controversial?

Dr. Bauer. Not to my knowledge, sir. I know of no official or unofficial complaints when we presented this area. There may have been some at the time of the study within the Public Health Service.

Mr. Fogarty. All right, Doctor, you have a prepared statement?

General Statement on Dental Services

Dr. Galagan. Yes, I have a complete statement for the record.

Mr. Fogarty. We shall file that in the record and you can summarize it.

(The statement follows:)

Statement by Chief, Division of Dental Public Health and Resources

Mr. Chairman and members of the committee, this year a new activity title, "Dental services and resources," appears for the first time in the budget of the Public Health Service. Previously, the activities covered by the new title were included, along with those of the National Institute of Dental Research, as items in the appropriation for "Dental health activities."

The appearance of the new title is in response to a request from the House Committee on Appropriations that the method of presenting the dental activities budgets be changed. In its report of March 25, 1960, the committee indicated that the method of presentation was no longer satisfactory. Stating that "the several components of the Public Health Service's dental program have become large enough and have sufficient complexity and importance to require separate budgetary consideration," the committee directed that in the budget for 1962, "the activities of the National Institute of Dental Research be carried as a separate appropriation item and separately defended and that dental public health and dental resources be separately identified."

The new title also is symbolic of the increasing strength and vitality of the dental programs conducted by the Public Health Service. At the time the report of the House Appropriations Committee was issued, programs in dental public health and dental resources were being conducted by two separate divisions, one in the Bureau of State Services, the other in the Bureau of Medical Services. On September 1, 1960, however, these two divisions were combined into a single organizational unit, the Division of Dental Public Health and Resources, an integral part of a logical sequence of total health activities designed to make more readily available to every citizen in every community not only enough of all types of care, but enough care provided in time to be effective. Consequently, the first appearance of the activity title, "Dental services and resources," which covers the program of the Division of Dental Public Health and Resources, signifies not only a new method of submitting the budget request, but the beginning of a concentrated, better staffed, more fully coordinated effort to solve some of the most critical problems in the field of public health.

The objective of the Division of Dental Public Health and Resources is to secure higher national standards of oral health and to do so by reducing the existing time lag between the discovery and the application of fundamental scientific knowledge. It seeks to achieve this goal by providing leadership and assistance to responsible public and private groups in the organization and administration of community health service at the State and local level. Attainment of this objective requires the development both of practical methods for determining the nature and extent of dental diseases and of more effective procedures for preventing and controlling them. It will require intensification of efforts to secure acceptance and application of prevention and control techniques already available, and it will require the building of a supply of professional personnel and resources adequate to meet the public's need for dental services.

THE PROBLEM

Few, if any, countries enjoy a higher standard of dental health than the United States does today; yet dental disorders are both the most common and the most neglected of all chronic conditions plaguing the American people. Fear, indifference, and ignorance of the need for treatment, together with the costs and inconvenience of seeking it, combine to create a wide gulf between the amount of care people need and the amount which gets translated into an active demand for service.

Each year, some 60 percent of the population receive no dental care at all and still others receive only the emergency services necessary for the relief of pain. The shocking result is that 3 in every 10 Americans past the age of 35, 4 in 10 of those past 45, and 5 in 10 of those past 55 are left with no natural teeth at all.

Now, however, the barriers to the receipt of care are being progressively lowered. As educational levels and living standards improve and as the population comes increasingly to reside in cities, more and more people seek a better standard of oral health for themselves and their children. The widespread interest in adding dental benefits to the health coverages now providing effective protection against other medical expenses provides heartening evidence that individual members of the population want and expect a more nearly optimum standard of dental health than prevails today.

Meeting the rising demands for service, however, will be an extremely difficult task. The number of dentists being graduated today is not much larger than it was a generation ago. But while a generation ago fewer than a million people were being added to the population each year, today 3 million are being added. By 1975, the annual increase in the population will exceed 5 million.

Because of the continuing failure to train dentists in numbers great enough to pace population growth, the number of dentists serving the civilian population has fallen from a previous high of 58 per 100,000 to only 46 today. As a result, dental school capacity must be expanded 80 percent within the next 10 to 15 years to maintain today's service levels. Formidable as this goal is, achieving it will represent at best only a partial solution to the manpower problem. Service demands are rising so rapidly that three times this rate of expansion would have to be attained if we were to make absolutely certain that the dental profession can meet future demands for care. For this reason, it is imperative to increase the effectiveness and efficiency with which the individual practitioner uses his time and skills. Otherwise, we cannot hope to assure that dental services will continue to be available to all who seek them.

Most critically serious of all, however, is the tragic failure to apply the preventive procedure now available. Specifically, we have not been able to convince community authorities that such dramatic technical developments as fluoridation of community water supplies are practical and feasible. We need to do a better job of mobilizing private and public health resources to apply the knowledge we now have.

It is within this setting that State and local health and welfare agencies, educational institutions, professional organizations and other groups throughout the Nation are attempting to develop programs to improve the dental health of the Nation. Vast as the problems are, however, the majority of the agencies charged with dental health responsibilities continue to work with inadequate budgets and insufficient numbers of personnel.

THE PROGRAM

This activity, aimed as it is toward stimulating and supporting regional, State and local efforts to improve the dental health of the Nation in a period of developing manpower shortage, is necessarily many sided. It focuses on a broad range of functions which encompasses disease control in the broadest sense—studying the magnitude of dental diseases in the Nation; developing methods to prevent the occurrence of dental diseases and conditions; promoting the use of dental disease prevention and control measures; carrying out a nationwide informational program; studying dental manpower needed to provide dental services today and 20 or more years hence; developing and promoting utilization of methods to make the most effective use of our limited manpower resources; and learning ways of overcoming the economic and attitudinal barriers which may prevent people from receiving needed dental services.

There follows a more specific description of progress made, current programs, and activities planned for 1962. For 1962, an increase of $89,300 over the 1961 level of $2,092,700 is requested. This increase will be used primarily to support activities related to the development of dental programs for institutionalized and homebound patients.

Fluoridation

Fluoridation of community water supplies is the most effective single method for preventing the occurrence of tooth decay, and, in all probability, will continue to be the method by which the largest numbers of people can obtain the dental caries control benefits of fluorides in the most simple, least expensive way. As of November 1, 1960, 37.9 million people in over 1,900 communities were served by water supplies supplemented with optimum amounts of fluoride. We can take little comfort in this record, however, for recently fluoridation has lagged behind population growth. A measure of our problem was revealed in the November election when 16 out of 22 communities defeated fluoridation proposals. One of the primary reasons for the failure is not hard to find. It lies in the continuing, well-organized, and evidently well-financed opposition of a vociferous, militant minority who fight fluoridation wherever it is proposed. Undeterred by scientific facts uncovered in years of research, antifluoridationists have drowned out supporters of fluoridation and have succeeded in turning a health matter into a political issue.

Within the limits of the resources available to it, the division proposes to intensify its support of fluoridation, providing a centralized program of education and information which can be effective in counteracting misstatements and half-truths.

Because the majority of public health personnel and scientists find it difficult to understand the underlying reasons for some community and individual behavior in relation to fluoridation, the division has stimulated a marked increase in interest on the part of social scientists in the phenomenon of community decisionmaking in regard to fluoridation. A number of social scientists in universities, health agencies, and within the division, are conducting studies which may provide the facts leading to a better understanding of the factors which influence people to react both positively and negatively to fluoridation. The implications of these findings for other health programs also are substantial.

Fluoridation is an economical and effective process, but work to make additional technical improvements in the process is being continued. For example, the technique and equipment for dissolving calcium fluoride in alum solution, developed in the division's laboratory, permits the use of the abundant, inexpensive, but highly insoluble compound fluorspar for community water fluoridation. Through the use of fluorspar, the cost of fluoridation may be reduced by at least 50 percent in water systems using alum as part of their treatment programs. Fluorspar dissolvers now are in operation in two small communities. However, since additional technical problems must be solved before the apparatus can be used successfully in large as well as small cities, a fluorspar dissolver will be developed and placed into operation in a medium sized or large community during 1962. Successful development and demonstration of the fluorspar dissolver in various sized cities eventually should lead to marketing of dissolvers by private industry.

In 1960, two projects were initiated to develop further the equipment processes, and organizational patterns for providing individual home water fuoridation services to individuals not served by community water supplies. In one community in which home fluoridation service is being offered by a commercial organization experienced in providing water softening and similar services, the response has been poor. On the basis of this short experience, it appears that people in the area (Will County, Ill.) find the $5 monthly service charge excessive, especially since they also require water softening services.

The second of the two projects is focusing on the development of a new type of fluoridation device which will reduce the cost of home fluoridation service. Using this feeder, the home water fluoridation service is expected to be offered to consumers in the Pittsburgh, Pa., area for only $1.95 per month. Successful development of this service may provide the major breakthrough in home fluoridation for which the Public Health Service has worked the past 5 years.

School water fluoridation is another alternative approach to community water fluoridation which is being tested in two Kentucky and Pennsylvania communities.

While fluoridation of water supplies still seems to be the most efficient means by which the decay preventive benefits of fluorides can be brought to the public, a number of other potential approaches are being developed. For example, studies are being made of the effectiveness of one application of topically applied stannous fluoride which may prove to be as effective, or even more effective than four applications of sodium fluoride—the compound generally used by dentists to prevent tooth decay. A new study to determine the potential for use of a new fluoride dentifrice in community health programs is being initiated and will continue into 1962. As other new findings which may have potential in public health practice emerge as a result of the basic research activities of the National Institutes of Health, universities and other agencies, additional studies and demonstrations will be launched with the objective of developing these findings further so that their acceptance and use in State and local health agency programs, and ultimately by the public, can be speeded.

The partial removal of fluorides from water supplies having excessive amounts is needed in over 700 communities having approximately 1.5 million people. The cost of defluoridation by methods already developed by the Division is about the same as for other water treatment procedures, but cost still remains a deterrent to defluoridation in many communities. During 1960, a laboratory model of a new defluoridation apparatus was developed. This device, similar to one used to refine uranium ores, is expected to reduce the cost of defluoridation markedly inasmuch as it is substantially automatic. Based on the expectation that tests of this model during 1961 will be satisfactory, a full-sized model then will be constructed in 1962 and tested in a community.

Individual health practices

The problem of understanding the behavior of individuals in relation to fluoridation is only one of the problems of this general type with which the public health worker and the private practitioner is concerned. Many recommended health practices go unheeded. For example, many people go to the dentist only when an emergency requires such action; however, it is recommended that individuals see their dentists routinely about twice a year. Many people fail to brush their teeth regularly, properly, or at a time it will do the most good; however, it is recommended that individuals brush their teeth immediately after eating.

In order to develop some better understanding of the reasons many important health practices are not followed, the division studied the attitudes and health behavior of individuals employed by the Endicott-Johnson (shoe) Co. of New York State. This group was selected because all employees of Endicott-Johnson Co. are provided dental services at no cost to themselves. Therefore, the cost of dental service as a deterrent to obtaining dental care would not be a factor in this population group. Although the analysis of the data is not complete, preliminary findings indicate that certain barriers within individuals prevent them from seeking regular care and that it seems possible to predict whether individuals will seek dental services on a regular, periodic basis if we know how they regard themselves in terms of susceptibility to dental disease, benefits to be gained from dental treatment, and other related beliefs.

Some of these findings will provide the basis for a study in 1962 of individuals who provide for their dental care through prepayment programs, and for more definitive investigations of the dental health practices of school children which will be initiated during the current year and continued during 1962. The 1961 level of activity will be maintained in 1962.

Community health practices

Intermittently over the past few years, facts relating to the personnel, financial support, and program content of State and local health agencies have been gathered and analyzed. These data, although extremely limited in scope and depth, serve as an invaluable tool for broadly evaluating the growth and development of health agencies and for identifying community health practices which are receiving major emphasis at any given time.

During the current year and continuing through 1962, an intensive program will be conducted to elicit essential information for assessing the current status of dental health activities in the United States and for developing long-range plans to cope with the Nation's unmet or emerging problems.

The evaluation of specific community health practices is an important area of responsibility. Always abreast of the latest dental public health evaluation techniques, the staff provides technical assistance to State and local health agencies interested in appraising program accomplishments. A community baseline survey of dental caries prevalence prior to fluoridation and five or more years subsequent to fluoridation is an example of one of these recommended evaluation procedures for which assistance is provided States and communities.

This year the Division contributed a new and important evaluation technique with the publication of an objective method for assessing oral hygiene status of individuals and communities. This technique, the "Oral Hygiene Index," can be used, for example, to determine the effectiveness of dental health education programs aimed to improve oral hygiene and to identify the relationship of oral hygiene to other conditions or disease entities such as dental caries and periodontal disease.

During 1962, the index will be used to determine whether community programs to improve oral hygiene status are effective in reducing the prevalence of periodontal disease. In addition, work will be continued to evolve additional important uses for the index.

Payment systems for dental services

The economic barrier to the receipt of dental care services by the public has produced, over the years, some interesting experiments with systems under which a greater number of individuals can meet the costs of dental care, either through budgeting payment in advance or after receipt of dental services or by participating in programs in which they share the cost of dental services with a union or other group interested in the welfare of the individuals.

However, for a variety of reasons, organized systems of payment for dental services have not grown as rapidly as those under which medical care services are provided. Today only 1 million people participate in programs which make possible the group purchase of dental services. It may be anticipated that these organized plans for financing dental services (which are the Blue Cross-Blue Shield plans for dentistry) will grow at a phenomenal rate in the next few years.

Preparing to meet the requests for assistance which inevitably will accompany this anticipated growth, the Division is engaged in the collection of actuarial data and in the documentation of facts concerning the evolvement and operation of various types of prepaid dental care programs. For example, an anaysis currently is being made of the structure and function of the four dental service corporations which are operating in Rhode Island, Washington, Oregon, and California. This information will provide the background required to develop a much needed manual of organization and procedures for use by the dental profession in establishing other dental service corporations.

To gain even more competence in this field, in 1961 the Division initiated a cooperative undertaking in Michigan to develop a program to provide dental services for various consumer groups through a dental service corporation established by the Michigan State Dental Association. Also cooperating in this undertaking are the University of Michigan and the Michigan State Health Department. This project will serve as a laboratory and will provide a teaching site for others seeking to gain experience in the operation of a dental service corporation.

The continuing Division studies of the development of payment systems and organizations for providing dental care services have furnished a background which enables Division staff to provide dental societies, State health and welfare agencies, and union and management groups with technical assistance and consultation in many phases of such program development. To support this effort, a National Clearing House on Prepaid Dental Care has been established within the Division. All information derived from the aforementioned factfinding and developmental activities is being brought together and made available for use by interested agencies and individuals in dentistry, labor, management, government, and the insurance industry.

During 1962, the information and data gathering activities will continue at the same level.

Manpower supply

The six regional manpower studies completed in cooperation with State and regional planning groups have focused attention on the increasing shortage of dentists and the needs for additional school construction throughout the United States. These studies also have led to the development of national projections of dentist needs in the United States to 1980.

Division staff have contributed substantially to the development of plans in some States for constructing dental and dental hygiene teaching facilities. In the States of Rhode Island and New Mexico, for example, technical assistance and consultation has been provided in establishing dental hygiene schools. Ohio, California, Pennsylvania, and Nebraska have been assisted in the alteration and expansion of existing schools and the planning of new facilities.

A survey of dental school facilities—of their space requirements, and space relationships—is being conducted so that the best possible use may be made of scarce construction dollars by avoiding a duplication of efforts by facilities planning groups and by assuring that every new school built will be modern enough to accommodate the latest advances in teaching concepts and flexible enough to permit future innovations. In cooperation with the American Dental Association and the American Association of Dental Schools, we are working to collect and evaluate the necessary technical data and are formulating recommendations and criteria concerning all phases of dental school space planning and utilization. As a result we soon shall be in a position to provide prototype plans, specifications, materials, guides, and other technical information to any interested community or institution.

A related series of studies is being conducted in order to increase our understanding of the financial plight of dental schools and of dental students. These studies, which will continue into 1962, should provide the basis for planning intelligent and comprehensive solutions to this problem.

As plans are made to increase the future dental manpower supply through the expansion of dental teaching facilities, it also is incumbent upon the dental profession to focus on the problem of attracting, as dental students, large numbers of individuals who have the potential for development into highly qualified, skilled practitioners. As opportunities for education in this country increase, and as new, interesting, and rewarding career opportunities in the biological and social sciences and other fields present themselves, it will become increasingly difficult to attract high quality students into dentistry in sufficient numbers to meet growing needs unless some definitive action is taken immediately.

Realizing that a comprehensive program of recruitment eventually will have to be developed by the dental profession, the Division is attempting to obtain a better understanding of some of the factors which influence students to choose dentistry as a career or which mitigate against such a choice.

As a first step, the Division has requested Rutgers University to explore the attitudes of high school students toward dentistry as a profession. In 1961, a study of dental school applicants is being initiated to identify the fatcors which motivated them to apply for admission to dental school and to compare dental school applicants with applicants of schools of law, medical sciences and other scientific fields. These studies will continue in 1962.

Manpower utilization

One of the known effective methods for providing more high quality dental services to more people, even under the extant adverse dentist-population ratio, is to use the skills of the dentist discriminately. But, to achieve such discriminating use, both the dentist and the auxiliary personnel he might use must be trained to work together.

Division projects to train dental students to use auxiliary personnel effectively have had the enthusiastic participation of 10 dental schools. In September 1960, a conference on utilization and training of dental assistants was held. At this conference, jointly sponsored by the American Dental Association and the American Association of Dental Schools, the experiences and the progress of the 10 pilot projects were discussed by representatives of dental education, and educational standards for dental assistants were considered. Spokesmen for the profession were clearly of the conviction that effective use of chairside assistants is one way to extend the availability of dental services.

Funds were appropriated in 1961 to the National Institute of Dental Research for training grants to support nucleus training activities in this field at all dental schools. Because the program is an integral part of our manpower and educational activities and a logical extension of our earlier experimental efforts, we are administering the program for the National Institute of Dental Research.

As more and more dentists are made aware of the benefits to be derived from using auxiliary personnel in dental practice, an increasingly large supply of dental assistants will be needed. It is estimated that at least 70,000 dental assistants adequately trained for chairside assisting should be at work by 1975 if dentists are to benefit from the training they receive. Today there are few well-trained dental assistants. To compound the problem, little experimentation has been done to identify the specific kinds of training needed by dental assistants, the optimum amount of time required for their training, and the settings within which the training should be provided. To develop and test alternative approaches to these unanswered questions, five cooperative programs have been launched in the setting of the dental school, vocational school, and junior college. These projects will be continued during 1962.

Dental services for handicapped children

According to recent surveys of State dental programs, little is being done to provide dental treatment services for the several million physically and mentally handicapped children in the United States. Even more disturbing is the fact that in the majority of States, no broad scale effort is being made to assess the dental problems of the handicapped child or to identify potential resources for providing needed dental treatment services. Continued denial of dental care services for these unfortunate children can only increase the burden of physical disability which they will carry into adult life. Fortunately, there now are available techniques which make it possible to provide dental care services for handicapped children. However, these advanced techniques have not been utilized to any great extent. Few dentists are trained adequately to provide treatment services for the handicapped child; there is little financial support for organized dental service programs for this special group; and there is an almost total lack of interest in developing actual and potential resources to solve this problem.

In 1961 two modest pilot projects were initiated in the States of Idaho and Illinois to develop organized approaches to providing dental services for the handicapped child—including the cerebral palsied, mentally retarded, and others.

Dental services for institutionalized and homebound patients

The institutionalized and homebound chronically ill and aged comprise another population group for whom little has been done to provide for their dental treatment needs. Here, too, the Division can and will give leadership and support. In an area too long neglected to permit quick and easy solutions, the Division is already providing a base for community action through studies which not only measure the extent of existing needs but which also aid in the development of techniques and the special training of personnel required to provide it.

A 4-year study we are just completing in Kansas City provides some measure of the problem. Out of 4,000 nursing home patients examined—their average age was 75—only 12 percent were not in need of dental care. The services they required covered almost the entire range of dental services: fillings, extractions, periodontal treatment, dentures. The number of the aged and infirm are increasing. Their need for dental care is too great to be ignored. Meeting those needs—meeting them adequately—is a central and immediate responsibility of dental public health and of the dental profession in general. We perhaps have a better opportunity today of fulfilling that responsibility than ever before. We are already initiating programs to provide a sound base for the development of community dental programs both for the aged and for handicapped children.

The requested increase of $89,300 over the 1961 level will be used to support a trio of activities related to the next phase of programing to meet the dental needs of the chronically ill and aged. A cooperative Federal-State-local program to provide dental services for the chronically ill and aged will be launched in a demonstration community; local workshops to disseminate information derived from Division studies will be supported; and a pilot project will support dental school efforts to develop curriculums covering the latest knowledge concerning the technical, administrative, and social progress which can be made in coping with the problems of the chonically ill and aged. These programs have the active support of the dental profession. It is of great importance to assure that dentists in communities throughout the country are taught how to employ the special techniques and equipment required to provide care to these disadvantaged people, to give them the benefits of essential health services which it is already possible—and necessary—to provide.

Career development

The career development program was developed in an effort to insure an adequate supply of well trained dental public health personnel for the Service. This program involves at least three types of assignments: (1) Supervised experience in a State health department; (2) supervised experience in a regional office; and (3) at least 1 year of graduate work at a school of public health.

During 1961 eight Public Health Service dental officers are attending schools of public health and pursuing advanced courses of study in public health and two dental officers are assigned to regional offices for training. In 1962 the program will be continued at the same level.

CONCLUSION

None of the studies, projects, or programs presented here have their conclusion in a list of statistics on a printed page. They have been and will continue to be augmented by programs in which technical assistance and consultative services are provided to States and communities by a staff of specialists and regional consultants. Facts, after all, have meaning only when they are employed and employed constructively.

There is certainly no area in which the constructive employment of every available fact is more necessary than in dentistry. Though we feel that our program is effective, the fact remains that we have as yet hardly begun to approach any real and final solutions to the dental problems of this Nation.

Perhaps the recent report of the Commission on the Survey of Dentistry in the United States best describes the scope and magnitude of the effort which must be made to narrow the gap between what is done and what could be done to improve the Nation's oral health. The commission calls for joint Federal, State, and local governmental and nongovernmental financial support for a program which, in 10 years, will cost $1 billion annually (a 20-fold increase over current expenditures). The commission, in its more than 70 specific recommendations, points up the need to (1) heighten public appreciation of the importance of dental care; (2) increase the number and productivity of dentists; (3) extend the fluoridation of community water supplies to its fullest practical extent; (4) find ways to provide early and continuing dental care for schoolchildren on an incremental basis; and (5) support, through grants, the development of State and community dental health programs.

The challenge the commission presents to the dental profession, to official and voluntary agencies, and to labor and business is great. While this report was published after our budget was already formulated, it is interesting to note that it offers direct support to most of our major activities in addition to identifying gap areas as yet untouched. Because the recommendations seem reasonable and appropriate in view of the job to be done, we shall make every effort, with the resources available to us, to meet that part of this challenge which has been directed to the Division of Dental Public Health and Resources.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Dr. GALAGAN. Mr. Chairman, as Dr. Bauer has indicated, this budget covering the new activity titles "Dental Services and Resources" stems, in part at least, from the recommendations of this subcommittee last year.

In compliance with your suggestion these programs were removed from the National Institute of Dental Research budget so this activity request does represent a new program grouping within the Public Health Service.

I should like very briefly to comment on the quantitative aspects of the problem with which we are concerned in this new Division. I am sure the members of the subcommittee are aware of the fact that it is one of magnitude rather than of mortal seriousness or as a cause of death. Dental disease affects every American almost continuously throughout his life. Consequently, we feel that our programs of prevention and control are of the utmost importance in trying to reduce the size of this problem to manageable proportions.

FLUORIDATION

Two examples of our activities related to prevention and control are the programs in support of water fluoridation and in support of the development of dental services for the chronically ill, the aged, and the handicapped.

As you know, fluoridation is one of the more controversial subjects with which the Public Health Service deals—controversal as a social issue, not in a scientific sense. Today fluoridation remains the simplest and most effective method of preventing a significant portion of tooth decay that develops in the American people.

The Public Health Service continues to put its principal emphasis in two areas in connection with fluoridation: First, we are attempting to improve the technical procedures for introducing fluorides into the water supply and making those procedures cheaper and more effective; and, secondly, we are attempting to stimulate interest throughout the United States in studying the social issues which are involved when communities consider fluoridation. We propose to continue our efforts in this area at the same level during the next year.

DENTAL SERVICES FOR DISADVANTAGED GROUPS

Equally in need of support from us are our programs designed to bring more dental services to certain disadvantaged groups such as the handicapped children and the chronically ill. Reports from several of our studies—one in the Kansas City metropolitan area in particular—give some idea of the programs we have been developing in the last few years. We have been able, in these programs, to determine the level of need which the chronically ill, aged, and homebound have for dental services. Almost every one of these people show an appalling amount of neglect.

In our studies we have been able to develop clinical procedures, portable equipment, and administrative and organizational methods for bringing dental services to these groups, whether they are in nursing homes, ill at home, or wherever they may be. We have been successful in developing methods for bringing those who are less sick to some central point for treatment. We feel that we are now in a position to move ahead.

The next step in the development of comprehensive community dental programs for this group, supported by the increase of $89,300 identified in this budget, will be used to accomplish three things in connection with the further development of dental services for the chronically ill.

We propose, first, to sponsor a statewide or regional conference of dentists and others concerned with the overall care of the chronically ills, such as nursing home operators, visiting nurses, and representatives of other associations. This conference would provide an opportunity for them to discuss mutually what might be done to develop a comprehensive dental program for the chronically ill within that area.

Secondly, we would propose to support a project in one dental school designed to develop methods for teaching dental students how to work with this disadvantaged group and to teach the use of the peculiar clinical techniques and portable equipment items that are involved.

Thirdly, we would propose to sponsor a pilot project in a demonstration community, which would be designed to show the community and the dental profession how they might organize themselves to deliver service to the chronically ill on a comprehensive basis.

DENTAL MANPOWER

Turning now to dental manpower, one of the more serious aspects of this problem continues to be the continuing decline in the Nation's relative supply of dentists. Our dentist population ratio is worse now than it was at the end of World War II and much worse than it was in 1930.

We have been, over the years, conducting a series of studies, regionally and in the Nation as a whole, designed to pinpoint the projected need for dentists. The results of these studies are and will continue to be available to groups who are planning the construction of teaching facilities for dentists. We plan to continue these studies at the same level during the next year.

We augmented these activities recently by a study of the dental school facility itself, of the physical plant, the space requirements and space relationships which exist in the present dental schools. We are doing this study cooperatively with the American Dental Association and the Association of Dental Schools. Findings from this study will enable us to provide planning groups, interested institutions, and communities with prototype plans, guide materials, and specifications which they will need as they move into the construction of the additional dental schools and teaching clinics needed to keep pace with the increasing demand for dentists.

Closely related to our interest in this area has been our concern about the utilization of auxiliary personnel in the dental field. Most particularly, we have been interested in the more effective and widespread use of the trained chair-side assistants who work with the dentist as a member of a team, just as the surgeon and his assistant work together. During the past several years we had developed some experimental teaching programs in a limited number of the dental schools around the country designed to train dental students how to work with this kind of an assistant.

These experimental projects were so successful that this past year, a modest program was initiated which would make available to every dental school a small sum of money to begin teaching the technique of working with chair-side assistants to the students while they are still in dental college.

This program is a logical and natural extension of our earlier experimental efforts and therefor we have been administering this training program for the National Institute of Dental Research this year.

I would like to mention briefly also the programs we have had for studying the various methods of financing dental care. The cost of dental service continues to be one of the major deterrents to the greater utilization of dentists.

Mr. Fogarty. What is the annual dental bill?

Dr. Galagan. It is about $2 billion a year.

DENTAL HEALTH INSURANCE

Mr. Fogarty. Why isn't dental care included in something like the Blue Cross coverage?

Dr. Galagan. We believe we may be on the verge of a real dramatic breakthrough in the financing of dental services. Even though the field has not developed the way Blue Cross and in Blue Shield have in protecting against sudden hospital and medical costs, there is every indication that the increased interest on the part of labor groups, the insurance industry and the dental profession will bring about such developments in the near future.

Many people in the insurance industry believe that dental coverage may be the next big development in the insurance field—that we will see, within the next 10 years, a rather marked increase in the number of people who are covered by some form of prepaid insurance for dental service.

In that connection we have been, over the past several years, conducting a series of research studies designed to identify the characteristics of these plans, determine their coverage, the benefits which are offered, their costs and the problems in adverse selection which they have had. Consequently a digest of information, a catalog of the experiences of existing plans in this field is available upon request to the dental profession, to industry, to labor, welfare agencies, or to any group that might be interested in using this system of purchasing or providing dental care. We propose to continue to conduct these research studies at about the same level during the next year.

SURVEY OF DENTISTRY

Lastly, I would like to call your attention to the report of the Survey of Dentistry completed by the American Council on Education. I don't believe it need be placed in the record.

Mr. Fogarty. All right.

Dr. Galagan. The Survey of Dentistry in the United States, representing an outside look at the dental profession, describes better than I the magnitude of the effort which needs to be made nationally to close the gap between what we presently do and what we can do to improve dental health in this country.

Of the more than 70 recommendations made by the Commission on the Survey of Dentistry, I should like to highlight five which I think are of primary significance for us in the Public Health Service. They are, first, to highlight and heighten the public appreciation of the importance of dental health and dental care through programs of education and information;

Second, to increase the number and productivity of dentists;

Third, to extend the fluoridation of community water supplies to its fullest practicable extent;

Fourth, to find ways to provide early and continuing dental care for schoolchildren on an incremental basis; and

Fifth, to support, through a system of Federal grants, the development of State and community health programs.

We believe this report by the Commission on the Survey of Dentistry stands as a significant definition of our national goals and aims in the field of dental health. Although our budget was prepared prior to the release of this report, I would like to point out that most of our major activities are fully in accord with the intentions expressed in this report.

In summary, Mr. Chairman, this budget calls for an appropriation of $2,182,000 which is an $89,300 increase over last year. I shall be pleased to answer any questions you may have.

REQUESTED APPROPRIATION FOR 1962

Mr. Fogarty. What did you ask for?

Dr. Galagan. From the Department, we asked for $2,459,000—an increase of $366,300 over last year.

Mr. Fogarty. Who cut it, the Department or the Bureau of the Budget?

Dr. Galagan. The Bureau of the Budget.

Mr. Fogarty. You think the Bureau of the Budget would change their minds if they had seen the results of this survey?

Dr. Galagan. That is a very persuasive document.

Mr. Fogarty. You still think you could use that additional money?

Dr. Galagan. Yes, sir; to develop further the programs that were described in this request.

PUBLIC EDUCATION FOR COMMUNITY FLUORIDATION

Mr. Fogarty. One thing bothering us, is that although the results of fluoridation are way beyond your expectations of 10 years ago, still 75 percent of the people in our country are not using it, and during the last year almost every referendum lost when it has come to a vote.

I would think the dental associations ought to be doing a better job in the educational field than they are doing. There is something wrong.

Dr. Galagan. Mr. Fogarty, we are very concerned with the lack of progress in the public acceptance of fluoridation throughout the country. I believe that the results of the November referendums, highlighted the problem we face. As I said earlier, the problem is not one of scientific character, but rather one of trying to understand the social issues that arise when the community considers fluoridation. After the November referendum, the American Dental Association issued several statements expressing its great concern about this problem. Also the Commission on the Survey of Dentistry called for increased emphasis on the promotion of fluoridation.

Mr. Fogarty. Do you have any ideas of what can be done to offset this trend?

Dr. Galagan. Yes, sir; I think there are three things we might do.

First of all, we could step up markedly our efforts to acquaint the public with the facts that are involved through our usual channels, that is the State and local health departments throughout the country.

Secondly, I believe we could increase the emphasis which we are placing on trying to determine why people act the way they do when they are faced with a group decision of this kind.

Thirdly, the Survey of Dentistry, in addition to the two activities I suggested above, also calls for Federal grants to support the purchase of equipment and the actual installation of that equipment in communities, particularly the small community which might be faced with some financial difficulty in getting the program started.

Mr. Fogarty. Sometimes it is a question of whether the local governing bodies put this question on the ballot. In some areas, the local governing bodies make that decision themselves. The town council or city council vote and take the responsibility; and in many of those cases they have fluoridation now, don't they?

Dr. Galagan. Yes, sir.

Mr. Fogarty. I don't think the AMA and ADA has done as much as they should in this area.

Dr. Galagan. The American Medical Association has, right from the very beginning, supported the program. The association has taken the position that their role was one of determining the effect of fluorides on the total health of the individual. Having assured themselves of the safety of fluoridation, the medical profession has left it to the dental profession and the American Dental Association to carry the ball in trying to make the facts known to communities.

SAGINAW

Mr. Fogarty. Do you know the problem they have had at Saginaw?

Dr. Galagan. Yes, sir.

Mr. Fogarty. I received a letter from the Director of Public Health about it. Did they make a real attempt to get it back?

Dr. Galagan. Yes. Saginaw is typical.

Mr. Fogarty. They had it, and then it was discontinued. They tried to put it back into effect again, and they were defeated.

Dr. Galagan. It is typical of a half dozen communities around the country where there is a small but active group opposing fluoridation. In these communities those opposing fluoridation have succeeded in getting it on the ballot and have often succeeded in defeating it and removing it.

Mr. Fogarty. Did the dental group in this area work very hard at it?

Dr. Galagan. Yes, they did, as did the State health department.

Mr. Fogarty. Sometimes they don't have time, because they are so busy, isn't that right?

Dr. Galagan. Yes. I believe it would be fair to say that the dentists around the country work very hard to try to acquaint the citizens of their communities with the potential of water fluoridation and to persuade the city governments that it is a desirable and effective way to prevent tooth decay.

There are individual exceptions to that generalization, of course, in the dental profession, but by and large, the Nation's 90,000 dentists have worked very hard at this program.

Mr. Fogarty. Well, as a dentist you, of course, would defend them. But I don't think they worked hard enough. I haven't seen much evidence of it anyway.

TOPICAL APPLICATION OF FLUORIDES

What about the average dentist in the country, in the rural areas where there is no chance of community fluoridation? Do they advocate topical application or have they forgotten about that?

Dr. Galagan. The topical application of fluoride has been available to the dental profession for more than 10 years now.

The use of this technique requires, in many States, that the dentist apply it himself. We have been proposing all along that auxiliary personnel be permitted to do this on a communitywide basis, on a group basis, so that one could reach large numbers of children.

Under those circumstances, it becomes economically feasible to administer this therapy.

Mr. FOGARTY. You think they could go to schools and do it there?

Dr. GALAGAN. Yes, sir.

Mr. FOGARTY. I live in a rural area so we don't have city water supply. But I don't hear of these dentists talking about topical application.

What about a child with very soft teeth? Would this topical application help?

Dr. GALAGAN. The topical application would be ideal for a person with teeth already erupted.

Mr. FOGARTY. I don't believe they talk much about it, do they? Maybe they do, but I very seldom hear any dentists talking about doing this.

Dr. GALAGAN. There are many dentists who use this procedure routinely in their practices. The dentist who concentrates on childrens' denistry uses this treatment routinely.

Mr. FOGARTY. This takes a little time.

Dr. GALAGAN. Yes. There have not been the developments in the community approach to this kind of treatment that we had hoped for.

HOME FLUORIDATION

Mr. FOGARTY. What about the individual home equipment?

Dr. GALAGAN. Well, as you know we have been working on home fluoridating devices for the past several years. There are two things of significance in the developments to date. We were able, in a demonstration area in Illinois to arrange to put an existing device on the market which would cost the consumer about $5 a month to buy.

Mr. FOGARTY. What is the total cost?

Dr. GALAGAN. This would amount to $60 a year.

Mr. FOGARTY. I see. It would cost them $60 a year?

Dr. GALAGAN. A service charge of $5 a month as you would rent a water softener or something like that. There was little interest in this service amongst the people in the area—it was essentially a farm area.

However, the other and more significant development, which we have been hoping would come through, looks now as though it may be a very real possibility.

We have been working with a water softening company in the development of a new device with no moving parts, no metal parts, a very simple, completely plastic device which could do the same thing as the machines which are more expensive.

The company reported to us last week that they have perfected this instrument and will be placing it on the market in the Pittsburgh area between now and the 1st of July.

Mr. FOGARTY. For how much?

Dr. GALAGAN. For $1.95 a month so that it would reduce the cost by about two-thirds.

Mr. FOGARTY. I would think in rural and suburban areas that there would be demand for something of this kind.

Dr. GALAGAN. Yes, sir; an instrument of this type and at this price or lower, we believe would be of real help to the people who find themselves in that situation.

SUPPLY OF DENTISTS

Mr. Fogarty. You say in your justification that each year some 60 percent of the population receive no dental care at all. Is it that high?

Dr. Galagan. Yes, sir. The national health survey has produced some very dramatic figures on the low utilization of dental services by the population in this country.

Mr. Fogarty. You also say that as far as our supply of dentists is concerned, we are worse off than we were in 1930.

Dr. Galagan. Yes; and also worse than we were in 1945–46; right after World War II.

Mr. Fogarty. Is that so.

Dr. Galagan. Yes.

Mr. Fogarty. So we are going backwards.

Dr. Galagan. Yes, sir; and unless we take some immediate steps to increase the productive capacity of the dental schools we will continue to be in poorer shape as the years go by.

ADA SUPPORT OF TOPICAL APPLICATION OF FLUORIDES

Mr. Fogarty. Does the American Dental Association encourage their dentists in topical application in areas where it is not possible to have it put into the water supply system?

Dr. Galagan. Yes, sir; the association has, right from the start, wholeheartedly supported these efforts.

Mr. Fogarty. I know they did at the start, but that is 12 or 13 years ago. Do you think they have lost interest?

Dr. Galagan. I think the American Dental Association probably has developed sharper interests in other vehicles for fluorides such as dentifrices, the home-fluoridation devices or tablets, all of which are designed to make fluoridation available to those who do not have a community water supply. The association has not neglected topical fluorides, however.

Mr. Fogarty. Have they tried to put some of these fluoridators in schools?

Dr. Galagan. Yes; we have two such instruments in schools. They have not been in long enough to demonstrate effectiveness in reducing dental cavities. They have been in operation for 2 or 3 years now and we are hopeful this approach will provide at least a partial answer to those who cannot get fluoridated water from the community supply.

DENTAL ASSISTANCE FOR DISADVANTAGED CHILDREN

Mr. Fogarty. What about these children you were talking about, those with cerebral palsy and mental retardation? Sometimes they are difficult to work on. Some dentists tell me that they take an awful lot of patience and time.

Dr. Galagan. Yes, sir.

Mr. Fogarty. The Office of Vocational Rehabilitation is supporting some projects along this line. We have one in Rhode Island. I think there are very few others in the country.

Dr. Galagan. You are speaking of the hospital in Providence?

Mr. Fogarty. Yes; where this care is made available to the cerebral palsy and mentally retarded kids.

Dr. **Galagan**. Yes, sir; but as you indicated there are very few such programs in existence in this country.

A recent survey of dental health programs in the United States revealed the appalling fact that very little is being done to provide dental care for this population. In 1961, Mr. Fogarty, the Congress made available to us a $50,000 increase which we used to support two pilot projects, one in Illinois and one in Idaho. These projects were designed to train dentists in Idaho in these particular techniques involved and to develop a statewide program of care for the handicapped children, the spastic and the cerebral palsy victim.

In Illinois, where they have had a training program for some time at the university, our efforts were designed to place emphasis on one or two counties and to support a comprehensive countywide service for these children. Thus we sponsored two different approaches to solving the problem.

Mr. **Fogarty**. You have been in it too short a time to have much in the way of results yet; haven't you?

Dr. **Galagan**. No. We do know it is possible to train and make available dentists who can provide services for these children. It is possible at the present time.

Mr. **Fogarty**. What about the cleft-palate problem? Are you doing any more in that field? Until recently not much was done about it.

Dr. **Galagan**. That is correct, Mr. Fogarty.

Mr. **Fogarty**. Is the Institute doing some work in this area?

Dr. **Galagan**. Yes.

Mr. **Fogarty**. Well, I will ask them.

Thank you.

Nursing Services and Resources

The next one is the Nursing Services and Resources.

Mr. **Fogarty**. Miss Arnstein, are you going to testify on this?

Miss **Arnstein**. Yes, sir.

General Statement

Mr. **Fogarty**. We shall put your full, prepared statement in the record here; and, if you like, give us a summary.

Miss **Arnstein**. All right, sir.

(The statement follows:)

Department of Health, Education, and Welfare

Statement by Chief, Division of Nursing on "Community Health Activities, Public Health Service," Nursing Services and Resources

Mr. Chairman and members of the committee, the nursing services and resources activity provides funds for a program which combines the operations of two former divisions—the Division of Nursing Resources and the Division of Public Health Nursing. This consolidation enables us to think and plan for nursing throughout the country in terms of total community health services regardless of where the nurse fits into them—in hospitals, in clinic, or in the home. All major ongoing projects of both divisions are being continued. And, by pooling personnel and other resources, we are finding it possible in some instances to strengthen certain activities which are able to benefit by the combination of two staffs. The 1962 budget request is for $6,525,000 for training grants and $850,000 for operations, an increase of $83,200 over 1961. This will enable us to make a beginning in the study of nursing care for the aged and to furnish additional consultant services.

All major problems in the field of nursing today fall into two categories—the need to deliver more care to patients, and the need to improve the quality of care provided. Work in this area is being done through research, consultation services, and grants for training.

The need at present is to extend nursing care services for the sick from the hospital into the home. Through consultation from its headquarters staff and regional office staff, the Division interprets to the health professions and to the general public the role of the public health nurse in new community health programs which are developing. These include care of the chronically ill, rehabilitation of the sick and disabled, and medical assistance for the aged. Consultation services are provided to State health agencies and to nursing organizations locally on questions of providing more and better nursing services of all kinds. Our consultants will also assist those responsible for launching and staffing new community nursing services.

In the last few months we have been giving special attention to plans for medical assistance to the aged. As the first step, we have developed some guidelines which have been sent by us to State health departments and by the Bureau of Public Assistance to their regional representatives. The 1962 budget includes allowance to complete a project which will enable us to appraise the effect of public health nursing patients.

Hospital administrators continue to be plagued by shortages of trained nursing personnel. Our earlier studies gave evidence that reassignment of clerical, messenger, and unskilled manual tasks would release many hours of nursing time for care of patients. One hospital saved $1,000 on one unit alone in a year by redistributing nursing skills and by assigning nonnursing tasks to personnel other than nurses. The Division is now refining its technique for studying nursing activities to enable more hospitals to use the study method. Over 200 hospitals have asked us to help them conduct these studies and to analyze the results. In 1962 we hope to adapt the methodology for specific application to the staffing problems of small hospitals. We also propose to apply the technique to the position of the supervisor, and to conduct studies in outpatient departments.

In 1962, we expect to have data from previous studies which can be analyzed to shed light on the extent and availability of the reservoir of inactive nurses in the country and the characteristics and work patterns of the many thousands of part-time nurses now being employed by hospitals. Using our census of public health nursing and existing data on hospital nursing personnel as bases, we also propose to develop a method of computing nurse supply and demand more accurately than has been possible in the past. Currently, hospitals are conservatively estimated to have 23,000 positions vacant for professional nurses; 55,000 public health nurses are needed for preventive and rehabilitation services as well as for home care of the sick.

This Division administers grants awarded for training under the professional nurse traineeship program and carries the responsibility for the nursing aspects of the public health traineeship program, as well as project grants to schools of nursing which provide graduate or specialized training in public health. The professional nurse traineeship program has grown from 56 participating educational institutions in 1957 to 93 in 1961. Over 6,000 nurses have received training aid under this program. A program of short-term courses was added in 1960 to begin to assist the more than 100,000 nurses in hospital leadership positions who desired special training but were unable to enroll in instructional programs of a full academic year. In 1½ years' operation to date, we have been able to award grants for 108 short courses which, in the first 12 months, provided instruction to about 2,000 nurses. The traineeship program is to be reevaluated in 1963 and the planning and data gathering for a national evaluation conference will be accomplished in 1962.

The increase we are requesting includes $21,000 to find out more precisely the amount of nursing care now being given to the aged. Data from such a study will give us a better base on which to plan future services for this important population group. An additional $22,600 is being requested for two new nurse consultants. They will work with those administering medical assistance to the aged programs, and will also assist local communities in the development of home nursing services for patients of all ages.

The budget as amended will provide for the establishment of an advisory committee on nursing education and nursing services. This committee will produce the data and recommendations through which the Public Health Service can take a position and make appropriate proposals to assure an adequate quantity and quality of nurses for the future. The increase of $40,000 will provide funds for travel and related costs for meetings of this group.

In closing, we believe that the organizational focus on nursing services, wherever delivered, made possible by the new Division of Nursing will provide; the optimum situation to study the fundamental problems of need, supply, and use of nursing personnel; the opportunity for the continued development of programs needed to improve and extend nursing services; and the emphasis and support required.

Mr. Chairman, I shall be glad to answer any question you may have about this program and the budget request.

Mr. Fogarty. Go right ahead, Miss Arnstein.

Miss Arnstein. I would just like to describe a few projects which we have now underway in the Division of Nursing which typify our work which, as you know, I think, is aimed at the expansion and improvement of nursing care.

This program will be continued at approximately the same level with the same general program, but with a slight increase for the additional consultation service and a special survey of the nursing care of the aged in their homes, and then in the amended budget there is a provision for the expenses of a special advisory committee to the Surgeon General to study and make recommendations on the educational nursing problem.

Mr. Fogarty. You think that will help, this advisory committee?

Miss Arnstein. We have great optimism.

We do think if we get an advisory committee on nursing to the Secretary and the Surgeon General with a multidiscipline membership representing hospital, medical, and nursing groups to consider their differences as well as their mutual goals, which are the same, that we could come out with a recommended program.

BENEFITS OF COMBINING NURSING RESOURCES WITH PUBLIC HEALTH NURSING

The nursing program, as you know, has experienced a major change this year in that the former Division of Nursing Resources and the former Division of Public Health Nursing have been combined and while this process I may say is a little difficult during the early months and a little time consuming, we think the end results will be well worth it and we are already noticing some benefits from the combining of the two divisions. They are not only benefits to us, but to the people we are serving.

For instance our title II nurse trainee program is often located in the same university where the public health nurse trainees are. Our consultants deal with both, and the university doesn't have to have two nurses. In the same way our State nursing surveys which you have heard about for some years now, we always thought were a little weak on the public health side and we hadn't given much time, attention, and thought to studies in the public health nursing field. We are now just getting busy on that and we hope in the years to come you will hear more about that.

I think that is enough for an example of how the two divisions' amalgamation will improve our services.

TRAINEESHIP PROGRAM

Now, as you know, our goals are to help get more nursing care and to get better quality care to the people.

The Division, in order to do this, will continue the traineeship program at the same level.

Mr. FOGARTY. What is that?

Miss ARNSTEIN. The title II traineeships as you know, have $6,525,000 and the title I has about half the total traineeships allotted to nurses.

We feel that in the title II which is training for teaching, supervision, and administration we are improving both quality and efficiency of the nurses. Under the title I we are getting more people with some training for public health.

ASSISTANCE TO HOSPITALS

The Division will continue to help hospitals improve the efficiency of their inpatient services, the nursing activity studies about which you have heard in the past, and we will, for the first time this year, stimulate the same kind of improvement programs in outpatient departments which have been rather neglected and are often the "stepchild" of the hospital and need help.

We will continue the attempt that we have just begun to find ways to help the small hospital. This is a very complicated problem because the nurse in the very small hospital does more than "double in brass." She is often the dietitian, the nurse, the social worker, and administrator, and sometimes the part-time pharmacist.

We are just feeling our way in this, but we hope in 1962 to go forward with it.

HOME NURSING CARE

We will assist communities to start programs of nursing care of the sick at home which is part of the total home health services which Dr. Knott was talking about this morning and for which his division is requesting the $1,960,000.

The Division of Nursing has been very active in this program through our headquarters and our regional office staff.

In promoting the idea, it has taken some educational work because for a good many years health departments thought they should only do preventive work and should not get into care of the sick, but because the present major health problems are chronic diseases, and as you already heard outlined because of the importance of the secondary prevention, which requires nursing services, there is a real change in the viewpoint of the local health departments and State health offices in the last year on this.

We have given assistance, primarily through technical advice, consultations and that kind of thing. There are more than 61 local health departments which have started nursing care of the sick in the home programs in the last 3 years. There are more than that—this is an incomplete report—but though 61 new programs is progress it is only a bare beginning.

Our regional nurses will continue to enlist support of community groups for this program.

There are some interesting examples if you want me to take the time——

Mr. Fogarty. Give us two or three.

Miss Arnstein. One of the first to have a very successful program that we heard of anyway was Du Page County in Illinois. They got some funds from the State health department which were Federal funds under the special "$2 million chronic disease" under general health grants and this community had been wanting to have a program of nursing care of the sick for some time.

With these funds, they were able to put on five additional nurses. Within 18 months they had put on another 10 nurses with community funds—that is to say the community was so impressed with the services that they raised additional funds of their own to carry on the service.

This year we had a report at the American Public Health Association meeting of a very rural county in California called Modoc and it was the county where our regional nurses had helped the State health department with the plans and so forth and in Modoc County it was too rural to give this kind of a service from the headquarters.

They found some inactive nurses living at home, married, not working at the time and they asked them if they would be willing—there were six of them spread around the county—to take care of people who became sick in their radius and these six nurses said they would do it.

They were sent to a visiting nurses association for 3 weeks training, brought them back to the county and gave them inservice training, and 6 months later some more training at a rehabilitation training center. This is where the Office of Vocational Rehabilitation centers fit into the health program because where they exist you can send people to get their training and patients to get expert help.

Now, these six nurses, under the guidance of the county public health nurse, a fully trained nurse, have been so successful that after 2 years, the county commissioners voted to take over half of the expense of the program this year and to take over the other half of the expense of this additional program next year so the State can withdraw its funds and put them in another county to start another program going.

This has been the usual experience; that once people feel the service is necessary they will support it themselves, but strange to say, they have got to feel it. They can't learn it from next door.

We do need more information on how to estimate the size of the caseload in counties of different types and different kinds and also on the financing and training of new personnel and this is one of the projects for which we have asked for an increase of money.

GUIDE TO STATE NURSING PROGRAMS

We have also this past year, in the interest of helping the States develop nursing care programs, prepared what we call a background paper or might call it a guide for the States health departments and the State welfare departments to use in developing their programs under the amendments to the Social Security Act that were passed last summer. This was done jointly with the Social Security Administration and they sent it out to their people in the regional offices at the same time that we sent it out to our people so that both Social Security and Public Health Service in the regional offices got it from their own headquarters people and have been using it in joint planning.

Mr. FOGARTY. You think the people in the regional offices have time to do anything about it?

Miss ARNSTEIN. They have, oh, yes. We learned from our regional offices as to what was going on in this joint work.

Mr. FOGARTY. They tell me they have so much to do now that they can't keep up with half the work assigned to them.

Miss ARNSTEIN. Oh, yes, that is true.

Mr. FOGARTY. I was wondering how you made out with them.

Miss ARNSTEIN. Our regional nurses are so overloaded that I have refused to ask for information that we need at headquarters. They are now the regional persons for the total program which combines the two former division programs, while until this year they had responsibility for only half the program. In addition to this they have placed the emphasis that we think is so vital on nursing care of the sick at home programs and they have agreed that this takes precedence over other important things. While they have accomplished much in this program they haven't been able to do other important things.

We have also prepared some short fact sheets which we have just sent out and which I thought you might be interested in.

These are just quickies to show what the program is and we think they will be helpful with community groups and appropriating bodies. All of this is being done working very closely with the Division of Chronic Diseases and other divisions in the Bureau.

NEW PROGRAMS IN 1962

The new programs in 1962 will be this survey of the nursing care that is now being given to older people; how many have received the care; what were their diagnoses; their nursing needs; how much care did they receive.

The second project is additional consultant help. That is two nursing consultants to assist the State and local health agencies in expanding these services that I have been describing and to help them in improving their hospital nursing services.

The third item is the Surgeon General's advisory committee.

I would be happy to answer any questions now that you might have.

ADEQUACY OF 1962 BUDGET

Mr. FOGARTY. What did you originally ask for? You ask in the budget for $6,525,000 for training grants. What was the original estimate?

Miss ARNSTEIN. The Department asked the Bureau of the Budget for $6,525,000 for traineeship grants and $839,000 in operating funds.

Mr. Fogarty. What did you ask for?

Miss Arnstein. The Public Health Service asked the Department for $6,825,000 in grants and $1,127,000 in direct appropriations.

Mr. Fogarty. Was that your figure originally?

Miss Arnstein. No, sir; we asked the Public Health Service for $1,437,500 for direct operations.

Mr. Fogarty. How much did you get?

Miss Arnstein. $850,000 in direct operations.

Mr. Fogarty. Has your advisory committee been set up?

Miss Arnstein. No, sir; they haven't been appointed unless there is some word today.

Mr. Fogarty. That is what the budget amendment of $40,000 is for, isn't it?

Miss Arnstein. Yes, sir.

Dr. Terry. It is in the process of being set up now, and before we can actually set up the committee we have to go through certain clearances which we are in the process of doing now.

Miss Arnstein. We are preparing for the committee now.

Mr. Fogarty. Last year we increased your budget request $600,000. Have you been able to use all of that effectively?

Miss Arnstein. Yes.

Mr. Fogarty. Could you have used some more money?

Miss Arnstein. Yes, sir.

Mr. Fogarty. Mr. Denton?

HOME CARE

Mr. Denton. I wanted to ask something about home care treatment. Who furnishes the doctor to treat these people?

Dr. Knott. Mr. Denton, sometimes the various home services include physicians and sometimes they do not.

Mr. Denton. What do you mean by "home services"?

Dr. Knott. Carrying medical services into the home.

Mr. Denton. What agency are you talking about; who is to provide that service?

Mr. Knott. In some cases the hospital; sometimes the health department itself—various agencies.

Mr. Denton. Who pays for this?

Dr. Knott. Sometimes the patient. They pay in accord with their ability to pay. Sometimes it is the welfare agency that pays the physicians.

Mr. Denton. If the man pays it himself, what have you gained? What has he that he didn't have before?

Dr. Knott. The organization of these services is such that services can be brought to him in the home. He doesn't have to go to a hospital.

Mr. Denton. But a doctor is willing to go to his home.

Dr. Knott. Yes, sir.

Mr. Dention. And if a doctor goes to a home anyhow, what have you added to it?

Dr. Knott. The home health services, Mr. Denton, consists of nursing services that go into the home.

Mr. Denton. I don't have a bit of trouble understanding the nurses going there.

Dr. Knott. The homemaker.

Mr. Denton. I understand the public nurse going in, but what I am having trouble with is how do you get the doctor in there?

Dr. Knott. The individual himself, Mr. Denton, may have his own physician.

Mr. Denton. If his own doctor would have gone in the home anyhow, and you get his own doctor to go to his home, what have you given him that he didn't have before?

Dr. Knott. Mr. Denton, the doctor, by himself, cannot provide all the services that the patient may need. This patient may need physical therapy. He may need occupational therapy or speech therapy.

If it is a woman, as the case I cited this morning, a woman with children, she may need a homemaker. The services we are talking about in home health service is augmental and supplemental to the care provided by the physician.

Mr. Denton. We have had public health nurses going into homes for a good many years.

Dr. Knott. That is right.

Mr. Denton. And what I am trying to get at is what you are giving them more than what they had before.

Dr. Knott. Miss Arnstein, you want to answer what the nurses do?

Mr. Denton. I think I know what the nurses do.

Mr. Ackerman. If I could give a layman's version I have had personal experience with a stroke case at home and naturally, we have a private physician but this person, after the stroke, was just sitting and was immobilized and the doctor wanted to get her out so he was able to call on the visiting nurse society to send the therapist in. They do wonderful work and we paid and were delighted to pay to be able to have these women come in.

Now, they have only two of those people for the whole city of Washington and it is terribly hard to get them because there aren't these services available.

Mr. Fogarty. You mean physical therapy?

Mr. Ackerman. Yes.

Mr. Denton. Who is going to pay them?

Mr. Ackerman. If you can pay, you pay, but the public welfare agencies pay for a large number.

Mr. Denton. Aren't you afraid you are running into socialized medicine there?

Mr. Ackerman. There are some welfare cases, of course, but the private people pay if they can, and as I say, we were delighted to pay the money to get the therapist in to help this person to walk.

Mr. Denton. I am having difficulty understanding this. What I am trying to find out is what you are giving them more than they had before.

Dr. Knott. They did not have these services before. There are over 200 cities with populations of 25,000 or more that have no visiting nurse service, let alone homemaker service or physical therapists to go into the home.

Mr. Denton. For a long time we have been trying to increase the visiting nurse services.

Dr. Knott. That is true.

Mr. Denton. And we all know pretty much what the visiting nurse does. I still don't understand what you have given them more than they had if their own doctor comes in and treats them.

Dr. Knott. The physician himself cannot give all the services that care today calls for, Mr. Denton. It is an organized system of home care. There is the matter of the homemaker.

Mr. Denton. The what?

Dr. Knott. The homemaker who can go in and keep the home together. There is the matter of the physical therapist; someone has to organize these services, Mr. Denton, and have a place where this can be coordinated. We are trying to stimulate communities to develop these services.

Mr. Denton. In my hometown who would organize that service?

Dr. Knott. It could be any one of the several agencies. It could be a hospital in your community; it could be a visiting nurse service who adds homemaker or physical therapy to their routines. It could be the health department; it could be a health and welfare council who develops these services.

It could be any one of several agencies.

Miss Arnstein. Fort Wayne, Ind., has had a project which you helped, Doctor Knott, I think for adding homemaker services to the visiting nurse services.

Mr. Fogarty. The difference is that the doctor is there for just a few minutes sometimes. He can't give speech therapy or spend an hour with a person trying to get him to walk a step or two a day.

Mr. Denton. Won't he tell them to get a speech therapist or tell them to get that kind of person that they need?

Dr. Terry. The point, Mr. Denton, generally speaking, is that those people have not been available and have not been available in an organized fashion.

Very commonly, yes, some of your schools and other institutions have that speech therapist but they have not been available in an ordinary community. The public health nurse in the past was concerned with the field of infectious diseases almost exclusively and as time has gone by we have felt the need and ability to use those people in other fields.

The visiting nurse today has a broader background and by having an organization within the community to supply these services, one can provide more for the population. The physician needs it to back him up.

Mr. Denton. I am not being critical. I am just trying to find out what you do.

Miss Arnstein. I think the center of the service is the nursing service, but as Doctor Knott says, it doesn't exist except in the larger communities. Some of the effort in these 61 places I spoke of are places that didn't previously offer any nursing care of the sick patient at home. The nurse carries out the physician's orders, she extends his services between visits.

Mr. Denton. Do I understand you are trying to increase the nursing services and trying to get speech therapists and homemakers?

Miss Arnstein. And physical therapists.

Mr. Denton. Is that what the program is?

Miss Arnstein. Yes.

SHORTAGE OF VISITING NURSE SERVICES

Dr. KNOTT. May I add a few figures to this discussion?

Mr. DENTON. Yes.

Dr. KNOTT. There are 200 cities with populations of 25,000 or over that have no visiting nurse service at all, Mr. Denton.

There are less than 50 coordinated care programs in existence serving a mere 5,000 people today. There are only 175 homemaker programs which would provide service to 3,000 families at any one time.

This is all we have in the country and you can count on the fingers of both hands the number of communities having these information and referral services such as we have in Providence, R.I.

Mr. DENTON. What is that?

Dr. KNOTT. An information and referral service is a central place where physicians or families that have chonic illness in their home can go to find out where they can get the facilities and services needed to take care of that individual.

Now, you speak of the physician going into the home. He isn't always aware of where the best place is to get the kind of services needed to provide the care for the patient in the home.

He may not know which is the best nursing home for this particular case. Nursing homes vary a great deal in the facilities and services provided and this central information and referral service can do much to help straighten out the individual that has a chronic illness in his home or the person himself who has a chronic illness.

Mr. DENTON. In my hometown we have a nurses registry service and they call to get a nurse. Is this something like that, only broader?

Dr. KNOTT. Much broader.

Mr. DENTON. I understand—like for a stroke case.

Dr. KNOTT. The arthritic is the same kind of case. Sometimes it is not the case of a nurse; sometimes it's just the case of coming in and seeing if the meals are prepared.

Mr. DENTON. As an example let's take a stroke case, did you use your own doctor there?

Dr. KNOTT. Yes.

Mr. DENTON. What did you provide that they didn't have, the visiting nurse and the homemaker?

Dr. KNOTT. Yes, and several therapists—speech, occupational, and physical.

Mr. DENTON. Who got all those people?

Dr. KNOTT. That came from the visiting nurse association in the case I cited this morning and it was through a coordinated plan of effort.

In other words, the nurse, physical therapist, the occupational therapist, and homemaker all outlined the specific responsibilities they had in that home in order to bring that patient back to a life of usefulness.

If these are not coordinated, and the speech therapist comes in not knowing what the physical therapist's or the nurse's aims are, this leads to a piecemeal type of care for the patient.

What we are hoping to achieve in these communities is a coordinated type of action for care of the patient.

ATTRACTING DOCTORS TO SHORTAGE AREAS

Mr. Denton. Let me ask you this. In the district I represent, there is one county badly in need of a doctor, and the question arises about how they can get a doctor in that community. They do have a visiting nurse.

Do you have any suggestion about any way they could get a doctor in that community?

Dr. Knott. I think they can go to the AMA which has a physician referral service.

Mr. Denton. They have done that.

Dr. Knott. Other ways in which communities try to attract physicians is to assure them a minimum income. In some cases, they provide them an office free of charge for a year. There are various ways.

Mr. Denton. In a county of that kind the people don't have a large income.

Dr. Knott. Many States have tried to find ways and means of encouraging physicians to locate in rural areas.

Mr. Denton. It seems to me there must be a great many places in this country where the same conditions prevail. There is no dentist in that county. The people have to go 40 or 50 miles to get to a dentist.

Now, it looks to me like that is a big field where some work could be done.

Mr. Fogarty. A mobile unit would be the answer in some places like that.

Mr. Denton. The mobile unit has been there for X-raying the lungs.

Dr. Knott. These could be organized by various agencies in the State. One of the ways in which Mississippi has attempted to answer this question of locating physicians in rural areas is to provide for the full scholarship with the understanding that upon completion of their medical course, the person agrees to locate in a rural area.

Mr. Denton. Who provides the scholarships?

Dr. Knott. The State of Mississippi. They have had some success. I wouldn't say complete success, but some success in locating physicians that way.

Mr. Denton. I don't think in Indiana we have many counties in that situation. This is the only one I know of.

Of course, that county has an $8 tax rate, and they would have a great deal of difficulty in issuing bonds to build a hospital. They thought about that but it wasn't practical. I have talked to the county commissioners on that phase of it.

I do think that is something that a great deal of thought ought to be given to—getting public health to counties like that. I am sure this isn't the only one in the United States.

Dr. Knott. Oh, no, sir; there are other rural counties. In North Carolina, in Person County, we are developing a home-care service there and again, this is a very rural area where the health department has taken on physical therapists, visiting nurses and homemakers and has endeavored to bring care into the home.

It does not provide for physician's services. The physicians are there.

ACCIDENT PREVENTION

Mr. DENTON. Now, on accident prevention. Have you done anything about designing highways so there won't be as many accidents? Have you given that any thought?

Dr. CHAPMAN. They have been busy on that for a long time. More recently they have been trying to design people so they will drive more safely.

One of the most interesting experiments that has been done was with the International Association of Chiefs of Police in Wisconsin. They have taken 2,000 stretches of highway and developed an electronic device which takes a picture of every car and designates its speed, its position on the highway, and so forth. Then they compare the accident rates on each of these segments of highways and where they are high, they will try, through enforcement, to change the traffic pattern to bring down the accident rate. In Virginia, they have done a tremendous amount of work on this. Where they find a piling up of accidents at an intersection, they study every foot of that highway and try to build out of that highway the danger spots. In one place they had 22 deaths. By simply putting in a middle lane in the highway leading to a left turn, they eliminated this danger spot.

Mr. DENTON. You do that work or does the public highways system?

Dr. CHAPMAN. The Bureau of Public Roads and State highway commissioners.

Mr. DENTON. That isn't in your field?

Dr. CHAPMAN. We work with them, with NIH. Our research grants are applicable to any area of highway research, whether it is design of roads or design of cars or design of people.

TESTING FOR DIABETES

Mr. DENTON. How do you test for diabetes?

Dr. KNOTT. We take a blood test, Mr. Denton to indicate the level of sugar in the blood. If it reaches above a certain point, 130 milligrams, that patient is referred to his physician for further testing.

Mr. DENTON. A urinalysis isn't made?

Dr. KNOTT. No, this is just a screening mechanism, sir.

VD REPORTING PROGRAM

Mr. DENTON. Dr. Smith, you stated that you had a program to have the doctors report venereal disease cases so you can find the source of infection and you were trying to encourage the doctors to report those cases to you more than they had in the past.

How are you coming with that program?

Dr. SMITH. This is going very well, Mr. Denton.

The private physicians are responding to this sort of appeal to meet their community responsibility and the number of early cases reported actually and comparatively each year is increasing.

We are happy with this program. It takes a lot of time and has to be done on an individual basis although we do try to present this program to as many conventions and as many medical meetings as we can.

Mr. DENTON. You have been very successful with that program in Atlanta?

Dr. SMITH. Yes, sir.

Mr. DENTON. What have you done to extend it to the rest of the country?

Dr. SMITH. At the present time there are programs in 15 States that are going very much on the Atlanta pattern that you are acquainted with.

TUBERCULOSIS PROGRAM

Mr. DENTON. Now, another thing is the TB program down there in Atlanta.

Dr. SMITH. The tuberculosis program is in Washington, not Atlanta. The administrative responsibility goes through the Communicable Disease Center at Atlanta.

Mr. DENTON. No change in that program then.

Mr. KELLY. The new buildings we are requesting funds for takes into consideration the housing needs for the tuberculosis program and until such time as we have the space, you could not move the people.

EMPLOYMENT OF DOCTORS FOR GOVERNMENT ACTIVITIES

Mr. DENTON. One last question. Do you people hire noncommissioned officers to do work for you in any cases?

Dr. KNOTT. Yes, sir.

Mr. DENTON. How general is that? I know you do in Indiana. Where else do you do it?

Dr. BAUER. Usually, we employ physicians as commissioned officers because there are many emoluments associated with this type of employment that a physician desires but there are many instances throughout the Service in the various programs where we use the civil service type of employment.

Mr. DENTON. You have good relations with the doctors?

Dr. BAUER. I would say, generally speaking, we have very excellent relationships; yes.

Mr. DENTON. I will tell you why I ask this. We have a report about social security and they have the State vocational rehabilitation review the claims and one of the reasons that was given to us for this was that vocational rehabilitation could employ doctors.

Are you in the same position to do that, to help the social security hire doctors if they couldn't get them otherwise?

Dr. BAUER. Actually, from the national program standpoint, in the Office of Vocational Rehabilitation a good percentage are on assignment from the Public Health Service. I think out of the five or six that they have all except one or possibly two are commissioned officers assigned from the Public Health Service.

Mr. DENTON. But that is in the regional offices.

Dr. BAUER. No, in Washington. In the regional offices the Office of Vocational Rehabilitation has two medical officers. Both of these have commissions in the Public Health Service.

Mr. DENTON. The State office of vocational rehabilitation official or officials have responsibility for reviewing these claims and they hire doctors to make physical examinations. Now, what I am trying to get at, is there any reason why vocational rehabilitation is better able to hire these doctors than you are?

Dr. Bauer. No; I would say to the contrary, except that at the State and local level, you hire part-time physicians to evaluate these cases. You can get part-time physicians at a local level much more readily than you can full-time physicians.

Mr. Denton. Are you in a position to hire them?

Dr. Bauer. Part-time physicians.

Mr. Denton. Suppose a district office of social security needed a doctor to make examinations of these claimants. Are you in position to help them with that?

Dr. Bauer. I would say this would be rather difficult because there are several positions available for every physician you can hire on a full-time basis.

Mr. Denton. Part-time doctors?

Dr. Bauer. Part-time doctors, I should think that they could hire them just as readily as the Public Health Service could.

Mr. Denton. Who could?

Dr. Bauer. The social security.

Mr. Denton. Hire them just as well as you could?

Dr. Bauer. Part time, at the local level area.

Mr. Denton. Does Vocational Rehabilitation have any advantage in hiring doctors that either you or social security don't have?

Dr. Bauer. I would say the Public Health Service has an advantage of two systems; one, civil service, and the other, commissioned officers.

Mr. Denton. One could do as well as the other?

Dr. Bauer. Yes.

Mr. Denton. That's all.

Mr. Fogarty. Mr. Michel?

STUDY OF NURSING CARE FOR THE AGED

Mr. Michel. Miss Arnstein, here on the first page of your testimony you mention an increase of $83,200 over 1961. This will enable you to make the study of your nursing care for the aged and to furnish additional consultant services.

Do you mean to say that up to this time, with all the nursing activity that has been going on in your section, no attention has been given to people in the elderly category? Or has this been broken down into categories of young people, middle aged, and so on?

Miss Arnstein. No, sir; we have given a great deal of attention to the total nursing care of the sick but the local visiting nurse service and health departments have not caught up to the times so they keep their annual reports by the following age groups, 0 to 1; 1 to 5, and then school age, then 20 and over. The beginning we hope to make in this study is introduce a finer breakdown of the 20 and over group into the 20 to 40 and so on—65 and over so we can get some figures on what is happening in the older age group.

Mr. Michel. What you are saying is that we are getting around to recognizing that, for elderly people, there are some completely different considerations that ought to be taken into account.

Miss Arnstein. Yes, sir.

NEW ADVISORY BOARD

Mr. Michel. A week or so ago I read blazing across the front page of my local paper: J.F.K. abolishes so many committees and boards. The general impression was that they were going to get rid of a lot of advisory committees. I notice in the last page of your testimony the increase of $40,000 will provide funds for travel and related costs for meetings of a new advisory group that hasn't even been appointed yet.

My first question: When will this new advisory board come into being?

Miss Arnstein. As soon as—well, Doctor Terry?

Dr Terry. Mr. Michel, this is an ad hoc advisory committee on nursing training and nursing education which is being set up by the Surgeon General for the purpose of studying present nursing training and education. This committee is in the process of being set up. It is the one we referred to earlier. We expect to have the committee report by the first of next year and presumably that committee, being a committee for a specific purpose, would be discharged after its report has been filed.

The primary objective is having something of a Bane committee, of the type of report as we had on physicians and physicians' training, education; to have this in the field of nursing.

This committee is being set up for this specific purpose and would be an ad hoc committee which presumably would be dismissed after it completed its chore.

NUMBER OF ADVISORY BODIES FOR HEW

Mr. Michel. How many other advisory committees and boards are there still in being in your entire field of operation?

Mr. Kelly. It's a tremendous number. The HEW is the leading Department in the use of advisory committees, most of which are scientific panels.

Mr. Michel. Were any of those affected by this recent order of the President to abolish certain committees?

Mr. Kelly. No, sir.

Mr. Michel. None in that category?

Mr. Kelly. None in the Department. We were participants in some that were interdepartmental but none of the departmental committees were affected by the order.

COST OF DENTAL SERVICES

Mr. Michel. Doctor Galagan, in the area of dental care, I was really surprised to learn of the increase in the number of people per dentist. I am wondering now of the cost of dental care. Is it in proportion to the decrease in the number of dentists?

Dr. Galagan. No; the cost of dental care has risen proportionately to the general rise in the cost of health services.

Mr. Michel. Cost to the patient, of course. That is what I am talking about.

Dr. Galagan. The cost of dental care has risen in proportion to the whole field of health care and even less than some of the other components. Hospital care, for example, has gone up at a much higher rate—almost twice the increase in dental care—but, generally speaking, the cost of dental service to the individual patient has increased at a rate somewhat less than the total health costs over the last 10 years.

Mr. MICHEL. Have you made some specific studies in this area?

Dr. GALAGAN. Not of the cost of dental care, per se, in relation to the total cost of health care.

Mr. MICHEL. I notice that there is an increase in the number of dental assistants. I have come in contact with this in my own dentist's office since they now do the work of cleaning my teeth and my children's teeth every 6 months. I can see that we are getting some place by having these people qualified for that purpose and not taking up the dentists time. But I am also very cognizant of the fact that the cost of cleaning my teeth hasn't gone down any with the decline of professional treatment, so-called, that I am getting.

Is there any comment in this area at all?

Dr. GALAGAN. I believe the greater use of all of those auxiliary to the dentist would extend the number of patients that the dentist can see, since he would be supervising less well trained people in greater numbers and hence they could all treat more patients.

I doubt very much if, in the final analysis, this would result in lower cost per unit of service to the individual. Rather it should make more service available to more people.

TRAINING AND QUALIFICATIONS OF DENTAL ASSISTANTS

Mr. MICHEL. What is the average length of the training these dental assistants receive? Is it 2 years?

Dr. GALAGAN. No, sir. The dental hygienist is trained for 2 years. The dental assistant as a profession is just coming on the horizon. The formal training which the assistants have been getting up until now has been on the order of 1 year.

Mr. MICHEL. Of college level training?

Dr. GALAGAN. Post high school.

Mr. MICHEL. And the average would be 1 year?

Dr. GALAGAN. Yes.

Mr. MICHEL. Now do these folks get a recognition certificate from the university where they take this training?

Dr. GALAGAN. There are a limited number of institutions (about 40, I believe) which make formal training available and which are certified or accredited by the American Dental Association and the American Dental Assistants Association.

Mr. MICHEL. But this does not mean then that every dental assistant has this caliber or grade of training or that formal qualification.

Dr. GALAGAN. No, sir, most of the dental assistants are trained on the job. This is one part of the problem which is in a state of flux right now as the dental profession tries to formalize the training which these girls have.

Mr. MICHEL. Do you anticipate in the future the setting up of a minimum standard as to what would qualify one for being a first-class dental assistant?

Dr. GALAGAN. Indeed so. As a result of our grant program to the dental schools for teaching dental students how to use assistants, we anticipate in the next few years that there will be an increased demand by dentists for properly trained dental assistants. Undoubtedly there will be more formalization of the training program for assistants, and broader certification and accreditation of these programs by the American Dental Association.

TESTING FOR DIABETES

Mr. MICHEL. Doctor Knott, in this matter of screening for diabetes, I know in your testimony that you say 1 percent of our population is screened at the present time.

Dr. KNOTT. At the present time.

Mr. MICHEL. And that you are working toward a goal of 4 percent.

Dr. KNOTT. That is right.

Mr. MICHEL. In answer to the chairman's question as to whether or not there was a cure for diabetes, I think your reply was in the negative.

Dr. KNOTT. I believe the question was preventive.

Mr. MICHEL. All right. Is there any way to prevent it?

Dr. KNOTT. No, sir.

Mr. MICHEL. What do we hope to accomplish then by the screening of 4 percent instead of one, and, if this increase is desirable, how much would you want to see that percentage increase above 4 percent? Would it ultimately be to screen everyone?

Dr. KNOTT. I don't think it would be necessary.

Mr. MICHEL. Would any purpose be served?

Dr. KNOTT. Screen everyone in the country? I think if we were to limit our screening to the high risk groups, Mr. Michel, for instance, those over 40, those who are obese, those women who give birth to progressively larger babies and particularly those who have had relatives with diabetes, I think this is where screening can yield the most fruitful results.

By early detection we firmly believe that we can prevent the development of complications. We can bring that patient under control more quickly and keep him in a longer state of health.

COMMUNITY ACTION TO PREVENT ACCIDENTS IN RURAL AREAS

Mr. MICHEL. Doctor Chapman, in the area of accident prevention, you stated in your testimony that in a rural area in Virginia, another type of community action is being taken on how to bring about the reduction on the incidence of accidents.

How would you go about this type of operation? Tell us about the specific example you cited in Virginia.

Dr. CHAPMAN. It is closing up in July, a sort of do-it-yourself job. For about a year, we sent a man into a 6-county area in Virginia and we got results weekly from 4 hospitals and about 96 physicians as to the number of people that came to the physician's office or to the hospital because of an accidental injury.

This set the base line. After that, we added a health educator and this public health advisor and educator used every available means of community organization to increase the interest and attention of people, old and young and in-between in the various causes of accidents.

They went to PTA meetings and clubs, and used radio, TV, newspapers, chambers of commerce, and so forth.

We had this sort of "do-it-yourself package" over a 2-year period. They found a very interesting phenomena; that is they got no reduction in accidental injuries in certain age groups but they got a 20 percent reduction in accidental injuries in the preschool ages and among the married couples from ages of about 29 to 50. This indicates that the family is an excellent place to do accident prevention education. They didn't find a way of hitting the age groups 6 to 30 by community education. Something different will have to be added.

There was no reduction in injuries to oldsters. This was interesting in that we found out how a small-scale, widespread operation can do some good at a very low cost. We will have to proceed to find out how to hit the teenage groups and the oldsters as well.

Mr. Michel. Doctor, I represent in part a large rural area and, of course, we have many accidents. Particularly brought to mind are men getting their hands and arms in cornpicking machines. I wonder in that specific kind of an accident, if the kind of a program you had in that area would be the answer. Do you think it is a matter of education?

Dr. Chapman. Our resources are so slim we cannot do everything we want to. I do not believe that education is a word we should use in preventing accidents. We should use the words conditioning and training. In other words, in our communities today we live at risk all the time. I saw a television spectacular 2 weeks ago on a Sunday where they showed a film depicting 6-year-old kiddies racing automobiles at 35 miles an hour. It shocked me at first but I realized after looking at it that the children had helmets on, they had seat belts on, they had rollover bars on the cars and they were trained to drive these cars safely, so no one was hurt. Wherever you see high-risk sports, the people who participate in them who are highly trained and conditioned are the ones least likely to get hurt.

This also applies to cornpicking machines. I hope some day to train an accident prevention team so that they can get out in the rural counties just as county demonstration agents do, go to the farms and attend specific meetings held for this purpose. There they can help to teach the people the specific dangers that they are likely to encounter, and how best to face them. We did that in one county, Mississippi County in Arkansas. There one public health adviser went in and studied every fire hazard they had. He found four major specific causes of fires. He went back to his office and built up some homemade props and used them to demonstrate to the people at these meetings how not to get killed by fire. They didn't know that if a fuse blew out this was a danger signal. What they did was to put in a bigger fuse. Then the house caught fire.

He has reduced injuries due to fires in 1 year better than 20 percent.

Mr. Michel. Is this the area you referred to down in Arkansas?

Dr. Chapman. Mississippi County in Arkansas.

Mr. Michel. It raises a question in my mind as to whether, on something so fundamental as what causes a fire—whether it is faulty wiring or a misuse of coal oil, and so forth—we would have to go into this kind of a program to inform people that this is what caused the fires. Is it that elementary a job that has to be done?

Dr. CHAPMAN. Yes. A member of our staff at a meeting last week said it was not faulty wiring, but a faulty use of good wiring. It is inadequate wiring is another way to put it. A housewife buys a new washing machine, plugs it in and the fuse blows. She has never been told that when the fuse blows it is an indication that the wiring is inadequate. So she puts in a bigger fuse and goes on using the appliance. The next thing you know, some time during the night or in the morning the house is on fire. Sometimes they burn up things through a very elementary lack of knowledge. They put wallpaper around the flue leading from the stove because the flue does not look very pretty. No one has told them that is a fire hazard. Simple things like that they do not know because they have never been told about it. A public health adviser can spot situations like that and brings them to people's attention.

SAFETY BELT CAMPAIGN

Mr. MICHEL. I notice your next item is the safety belt campaign When I had them installed in my wife's car, it came to something like $45, which kind of irked me. Then just last week a very good and close friend of mine was in an ordinary automobile accident which caused only a dent in the fender of the truck involved, and his own car wasn't badly damaged. But through some quirk, the car was whipped around and he, having no seat belt on, went through the back window. Not the windshield, but the back window, and he was killed. The use of seat belts in this kind of an accident, the State police said, would have saved his life, with no more than probably a few bruises.

Have there been any studies on the costs in this area of seat belts. I ask that because I can see, in a highly competitive business such as selling automobiles, the customer might see that it makes a difference of $45 or $50 and because of that would buy a different car. If the $45 or $50 difference is caused by a little matter such as seat belts, that could be the determining factor in the sale. If they put safety belts in every 1961 automobile wouldn't that bring the cost down, so that for $15 you could get that little piece of canvas with a couple of bolts and fastener attached to it?

Dr. CHAPMAN. The president of one of the larger automobile companies said that his company would install the fixings in the factory. He also asked all of his dealers to install seat belts at cost. The installation cost would be greatly reduced if the fixings were put in at the factory, and you merely had to screw in eye bolts. Then you could buy the seat belts wherever you want to and just snap them on. This is a major breakthrough which will greatly reduce the cost of installation. The other automobile manufacturers are following suit.

SAFETY-TYPE MEDICINE CABINETS

Mr. MICHEL. That is very good.

You pointed out to us the picture of the new safety-type medicine cabinet that children could not open, and evidently some of the manufacturers have taken an active interest in producing this kind of cabinet.

Dr. CHAPMAN. Yes, sir. I wrote to the president of the American Proprietary Drug Association and asked him if he could help us. He got the plumbing fixtures industry to cooperate, since we did not have the necessary money. They got the manufacturers of safety cabinets to conduct experiments. They were very much interested in this and they never made any charges. In a year's time they have developed standards which will be set by industry—they are not Government standards—for safety medicine chests. They have set up a set of criteria by which any new locking device can be evaluated. At a meeting held 2 weeks ago three different locking devices were exhibited, and three others are in the process of development. If you go home tonight and look in your own home—and I feel sure that this is true of most everyone—and you see all of those poisons and household materials lying around, it will be quite a shock to you. Where would you put them if you wished to store them safely?

There was a little cartoon in the Sunday paper that I saw. A man had a wall safe in the bathroom and he was saying to his wife, "Don't put money in there. That's for medicine." I cut it out of the paper because it well illustrated the point of having some safe place to put those dangerous materials into. Nor do household poisons belong in the kitchen. There should be a safe storage place in the garage for paints, turpentines, and other similar materials.

CONFERENCE ON DRINKING AND DRIVING

Mr. MICHEL. I notice there will be several national conferences held, one of which will be on drinking and driving. What would be discussed at a conference like that?

Dr. CHAPMAN. I talked to our Advisory Committee about that and said we seemed to be talking all around the core of the traffic accident problem. There is evidence which is not conclusive but presumptive that at least 50 percent of the people who are in fatal traffic accidents have been drinking. It was the Committee's decision after we presented the evidence that we ought to have a conference at which the experts on the subject would lay out on the table all of the known facts on the subject. I have some material here which I think would be of interest to you. It will just take a minute, if I might.

Mr. MICHEL. What do you do with all of the facts and figures you collect? How does this get to the people?

Dr. CHAPMAN. Through publicity and information.

Mr. MICHEL. Are there people attending this kind of a conference who will put this material into actual practice?

Dr. CHAPMAN. Yes, sir.

Mr. MICHEL. I recall on New Year's eve seeing ads in the paper saying that your last one for the road should be coffee, and things like that, which probably strikes a responsive chord in a good many minds. However, is there actually a goodly number of people who can put this material into practice, and who attend these conferences?

Dr. CHAPMAN. We want to lay the problem on the table so that researchers will realize the enormity of it and be inspired and motivated to go out and try to find answers to this very complicated problem. Obviously prohibition is not the answer.

Mr. MICHEL. No. I agree with that.

Dr. CHAPMAN. But there is an answer to every problem if you look for it deeply enough, and if the right people look for it. In the Low Countries they developed one method which may or may not work. When three or four people go out to drink one person does not drink, and all of the others drink what they want. The one person who doesn't drink brings them all home. I do not know whether that practice will stand up or not, but there are answers to every problem and before you can solve a problem you first have to be aware that there is a problem. I do not think that the American people realize the enormity of the problem.

DRIVING ANALYSIS

Mr. MICHEL. One last question to you, Doctor, and that is with reference to the analysis of the task of driving.

Dr. CHAPMAN. Yes, sir.

Mr. MICHEL. What is that all about?

Dr. CHAPMAN. When you go into an industrial plant you notice that every bit of equipment is designed so that the person who moves a lever moves it in such a way that in effect they are all natural movements of the arms and legs, or whatever parts of his body he uses. That is the result of human engineering and good machine design.

In automobiles we do not know what problems the driver has to face both within and without the car, in order to do the job he is supposed to do. So with that as a basis, how can we possibly find out if he is capable of doing the job until we know what the job is that he is supposed to do? Therefore we are letting a contract this spring with a research firm to give us the outlines of the total research problem, and as research opportunities become available to us we will tackle these problems one segment at a time.

For example, do we know what the effect of headlight glare is on different kinds of people at different times of the night and under different road conditions?

Up in Connecticut they put in overhead lighting on a highway 26 miles long and deaths dropped precipitously.

The design of the automobile must be studied to see whether the man and the automobile are properly matched, and whether there should be some changes in design. For example, is a pushbutton system safer than a gearshift lever? Can high seats or low seats bring about better driving?

Dr. McFarland made a study of trucks. He found in one truck that the seat was so low that the person could only see over the top instrument panel with difficulty. This reduced the field of vision 50 percent. We do not know enough about the task of driving itself, and what is required of the driver.

GRANT TO INTERNATIONAL ASSOCIATION OF CHIEFS OF POLICE

Mr. MICHEL. I noticed in the hearings last year—I was not a member of the committee at that time—Mr. Laird of Wisconsin was a little bit critical about one of the grants that had been made, I believe to the International Policemen's Association, or some such organization.

There were some rather vague answers to the questions that he asked.

What has happened under that grant?

Dr. Chapman. The International Police Chiefs' Association program in Wisconsin is the program I mentioned. It has already developed a method of traffic evaluation using electronic methods and a 650 IBM computer. This method tells exactly how many cars have passed over the road, what position they are in, and what speed they were traveling at. The number of accidents in each segment of highway is known. When they get through with this analysis they will take a high-accident area, study it and try to redesign the traffic flow to see if it will bring down the accident rate on that particular stretch of highway.

This is a very ingenious and very promising lead in the highway research field.

Mr. Michel. Since Mr. Laird does come from Wisconsin and was rather critical, is there more than coincidence between that and the fact that the study is out there in Wisconsin?

Dr. Chapman. No, sir. We have no control over the applicants for our research projects.

AIR POLLUTION

Mr. Michel. Dr. Shafer, in the grants to the States under this item of air pollution I would like to ask some questions. What States have taken advantage of that?

Dr. Shafer. I cannot answer that specifically, Mr. Michel. I would have to submit it for the record.

Mr. Michel. If you would simply supply it for the record, that will be all right.

(The information requested follows:)

The following States are using general health grant funds in organizational units of the State health department which are responsible for air pollution activities:

Connecticut
New Hampshire
New Jersey
New York
North Carolina
Ohio
Pennsylvania
Washington
Alaska
Hawaii

PUBLIC HEALTH SCHOOLS

Mr. Michel. You say there are 12 schools of public health receiving grants, an increase of 1 over last year. Which is the new one?

Dr. Shafer. The new school was the University of California at Los Angeles.

Mr. Michel. Do we have any in Illinois, by any chance?

Dr. Shafer. No, sir, we do not.

MIGRANT LABOR

Mr. Michel. I do not know who it was that answered in response to the chairman's questions relative to migrant farm labor, but I think you said you could use $250,000?

Dr. Shafer. Yes, sir.

Mr. Michel. And conceivably $2½ million to do a really thorough job. Am I correct in that?

Dr. SHAFER. We asked in one of our budget proposals for $250,000 for our own direct operations, and we feel we could use $2½ million for State and local health departments to meet this problem. We would propose that the $2½ million be made available for project grants to State and local health departments.

Mr. MICHEL. I believe you mentioned that California was doing something in this area, did you not?

Dr. SHAFER. They have quite an active program because they have a serious problem.

Mr. MICHEL. Right. How about some of the Southern States where the problem also exists. Are they doing anything?

Dr. SHAFER. Texas is doing a limited amount of work. It is the State with the second largest problem. Florida has been quite active in the migrant labor problem through the years, and has done a great deal of work in improving housing standards, and has worked with us in surveying some of these disease problems of migrants. Florida has also worked with us in improving the transportation standards for the migrant labor group.

Michigan has serious problems and they, too, have been doing a good job in improving health conditions in that State.

Mr. MICHEL. But you still believe that there is a very definite problem in the area of health?

Dr. SHAFER. I feel we are just at the point of a breakthrough where we know the problem and we know what needs to be done. Now we need the resources to do the job.

Mr. MICHEL. Regarding health standards you would set as a minimum for migrant farm laborers, would they be any different than any standards you might set for people in a large metropolitan urban center?

Dr. SHAFER. We would sincerely hope to bring the migrant farm labor up to the standards that are now met and surpassed by the people in metropolitan areas. By and large, the migrant laborers come from rural areas that have inadequate health services at the present time.

MOBILE HEALTH UNITS

Mr. MICHEL. Had you given the committee your judgment as to the feasibility of using mobile health units?

Dr. SHAFER. No. That was not discussed, but it certainly is one important factor in providing services to the migrant workers and their families. We have found that the regular clinic schedules, even in areas where they have available health services, are such that the workers are in the field and cannot get their families to the clinics during the day. So it is a question of either setting up night clinics or taking the clinics to the field. I think that the mobile clinic would be a real improvement in providing these services.

Mr. MICHEL. Would it be a feasible project?

Dr. SHAFER. It certainly would.

Mr. MICHEL. Do you feel we would be getting more for our money through the utilization of a mobile unit system?

Dr. SHAFER. This is difficult to answer, but it is the only solution in terms of getting services for certain areas. I think experience has shown mobile clinics do tend to be an expensive type of operation.

Mr. Michel. In that $250,000 you were talking about, is that taken into account at all?

Dr. Shafer. No, sir, it was not.

Mr. Michel. How about in the $2½ million figure?

Dr. Shafer. With the $2½ million; if some State health department or local health department wanted to include funds for a mobile clinic, then I think this would be possible.

Mr. Michel. With the $2½ million figure, how many States do you think could be satisfied?

Dr. Shafer. I doubt that we would satisfy all of the States. The problem is located principally in about 30 of the States. Again, we have States where there are high concentrations of migrant workers. We could undoubtedly satisfy the majority of them with $2½ million, but again, as you work through a problem you learn more about how to meet the needs of these people, and I am satisfied that experience would show we could possibly utilize even more funds. However, this amount would provide for a good start.

Mr. Michel. That is all.

NEW HOSPITAL DESIGN

Mr. Fogarty. I have just one further question, Miss Arnstein.

A few days ago I had lunch with a couple of doctors from the Mayo Clinic, and they are interested in a new design for hospital construction. I do not remember all the figures, but I told them to drop me a line with regard to it. I have not received the communication yet, but they claim that in the average hospital there is about 20 percent of the population of the hospital who require high-cost, intensive medical care. After a study they determined they could bring down the cost in that 20 percent from about $54 a day down to less than $20, I think it was. And they also told how they could bring down the number of nurses required by this circular type of unit.

That is a design where the nurse stays right there in the center, and she can see in every room, and the patients can see her. Have you given that any consideration? Have you spent any time on hospital construction or design in order to determine how you can make the nursing care go further?

Miss Arnstein. Both yes and no. We work very closely with Dr. Haldeman in the hospital and medical facilities. On this study we have not worked nearly enough, and I think Dr. Haldeman has heard me say in the past that I have an intense desire to find out whether either this circular design or a somewhat larger nursing unit, where the patient can see the nurse a great deal of the time, would prove to be a better design.

Mr. Fogarty. In this unit the nurse can see every patient. Can you see it in this design I am holding? The nurse is stationed in the middle.

Miss Arnstein. It looks ideal to me on paper but I have heard some criticism of it and I do not believe there are any studies on it from the standpoint of the patient's reaction, and the nurse's reaction, and the whole thing.

Mr. Fogarty. No. What they want is some money for four or five pilot studies.

Miss Arnstein. Experimental units.

Mr. Fogarty. They want to have these units built in different geographical areas and to carry their studies out. I think that was what they have in mind.

Miss Arnstein. We would like that very much. I think you may have heard Mrs. Adams last year in the Division of Nursing Resources talk about an experimental unit built for nursing experiments. But it is expensive to build an experimental unit so I do not think it should be confined to nursing experiments, but should include other types. You can build units apparently with ways of removing the walls and changing things around so that within the same outer structure—you can experiment with different patterns of care, and in that way find out do the patients sleep better? Do they ring their bells less often? Are they better satisfied with their care? Is the nursing more efficient? The physicians may have some ideas about this too, but we are very eager to do it.

Mr. Fogarty. Thank you very much.

Miss Arnstein. Thank you.

Note: Following is the formal justification for the budget amendment discussed in the foregoing hearing, and two statements submitted at the request of the committee:

RECENT DEVELOPMENTS IN THE USE OF FLUORESCENT ANTIBODIES

The major accomplishments during the first 6 months of fiscal year 1961 in the fluorescent antibody technique relate to its application to streptococcal disease. Beta hemolytic streptococci are the forerunners of rheumatic fever and nephritis. Conventional laboratory techniques take about 48 hours to arrive at a conclusive diagnosis. Using the fluorescent antibody technique a diagnosis can be made in about 3 hours if the equipment is readily available. Training courses at the CDC have now equipped at least one person from each State to do the test. At least one laboratory in each State now has the equipment to do the test. Three commercial houses are now manufacturing fluorescent antibody conjugates for streptococcus grouping. This combination of available reagents, trained persons, and equipped laboratories should lead to major improvements in the control of rheumatic fever, and hopefully a reduction in morbidity and mortality from this disease.

A field evaluation of the fluorescent antibody technique for detection of pathogenic coliform bacteria which cause infantile diarrhea was carried out in an endemic area in Puerto Rico. The data shows this test to be a valid and reliable one for the rapid diagnosis of disease caused by these organisms. Procedures and reagents will be made available to State laboratories.

An evaluation of a new fluorescent antibody technique for identification of diphtheria bacilli was carried out in conjunction with the Georgia State Laboratory. Considerable progress has been made toward the rapid diagnosis of diphtheria by the staining of nasopharyngeal exudates with fluorescent antibody, but more work is needed.

It has been shown that brucella bacteria can be stained specifically in culture and in tissues of experimental animals. During an epidemic of brucellosis in Iowa, fluorescent antibody tests were used to demonstrate the presence of antibody in the sera of more than one hundred patients.

All three types of polio antibodies have now been labeled with fluorescein successfully. The technique has been successfully used to identify unknown viruses in tissue culture at the CDC. While this application of the fluorescent antibody technique has not yet reached the stage where it can be done as a routine, when it does go through further development it should greatly speed and simplify the problem of polio diagnosis.

Fluorescent antibody staining techniques have been developed for the rapid diagnosis of the fungus *Sporotirchum schenkii* directly in pus from human cases. Progress has been made in the diagnosis of histoplasmosis by staining the causative organism from humans and animals.

Fluorescent antibody diagnosis of rabies has been evaluated and adopted as an adjunct test in several State laboratories. The test has proven to be remarkably specific and gives diagnostic results in less than a day as compared to two or more weeks for the mouse inoculation test.

The fluorescent antibody tests for gonococcal infection and syphilis have been thoroughly evaluated in the laboratory and demonstrated to be more sensitive and specific than previously available methods.

CDC has now initiated 14 studies in universities, hospitals, and health departments in the application of the fluorescent antibody technique for the detection of gonococcal infection. The breakthrough in the discovery of gonococcal infection by this method in a high percentage of asymptomatic females makes possible the detection of heretofore unknown foci acting as a source for spread of gonorrhea to the male population. Improvement in diagnosis of gonococcal infection in the female is permitting development of diagnostic and improved treatment procedures which should make possible significant progress in the control of gonorrhea.

Several medical school research laboratories and State health department laboratories with CDC cooperation are applying the test for syphilis to diagnostic problem cases. An international comparative study on the test for syphilis is being conducted in six foreign countries in cooperation with CDC.

The fluorescent antibody technique during fiscal year 1961 has been adapted at the CDC so that by measuring quantitatively the fluorescence of specific antibodies ameba can be differentiated. Using this technique it has been possible to show that the large and small races of *E. histolytica* are different protozoa antigenically. This may lead toward better understanding the pathogenesis and epidemiology of amebiasis.

Toxoplasmosis has in the past been an extremely difficult disease to diagnose. The tests available are cumbersome, and only done in a few laboratories. The fluorescent antibody technique has now been adapted to this disease. Experience in CDC training courses has shown that a person familiar in the general concepts of fluorescent antibody work can be trained to do the test for toxoplasmosis in one afternoon, and that the results will be comparable to those obtained from more cumbersome methods.

One commercial company is producing the reagent for rabies diagnosis and another is offering conjugation service to laboratories who provide their own sera. Several commercial laboratories are actively developing programs for producing a number of other reagents for diagnostic and research use.

Training courses in the technique are continuing at the CDC. A manual on fluorescent antibody techniques was prepared and is available from the Government Printing Office. Reference reagents have been made available to 46 States and 22 laboratories. Information on instruments and equipment has been provided to the State laboratories.

ACCIDENT PREVENTION ACTIVITIES

Funds	1960	1961	1962
Research grants	$1,125,265	$1,482,000	$1,921,000
Direct operations	401,400	1,440,300	1,447,000

The Public Health Service continues to take cognizance of the leading position of accidents among causes of death and disability. Ranking in fourth place among all major killers and in first place among killers of children above 1 year old and among young men and women through age 35, accidents exacted a toll of 92,080 deaths in 1959 and approximately 46 million injuries each year.

Although it is relatively new as a major activity of the Public Health Service, accident prevention can already demonstrate that by treating accidents as a major disease and applying traditional public health methods, we can effect a substantial reduction in the accidental death rate and both the number and severity of accidental injuries. In organizing and pursuing its accident prevention activities, the Public Health Service has been careful neither to usurp nor to encroach upon areas either outside the reasonable scope of public health interest or now adequately pursued by other governmental or nongovernmental agencies.

While the full impact of the economic costs of accidents, in terms of man-hours of productivity, might be considered outside the legitimate interest of the Public Health Service, the staggering medical costs are not. These costs are reflected in such statistics as, in 1 year: 38 million persons requiring medical care because of accidents; 11 million persons incurring accidental injuries requiring bedtime; 1,700,000 persons admitted to hospitals and utilizing millions of hours of scarce medical, nursing, and health technicians' time and a total of 50,000 hospital beds for an entire year.

It is interesting to note the comment of Gov. Howard Pyle, president of National Safety Council, in the National Safety Council publication "Safety in the 60's," that accidents in the decade 1950–60 cost the American people about $100 billion.

PROGRAM ACCOMPLISHMENTS

While specific accomplishments have been achieved in the brief career of the expanded PHS accident prevention program, the willingness of additional support on the part of many National, State, and local agencies, which heretofore have not participated actively in accident prevention activities, will have an even more profound effect on the success of accident prevention programs in the long run. It may be worthwhile to consider some of these at this time.

One of the most significant accomplishments is the increasing interest among State and local health departments in the application of public health methods to the problem of accidents. While accidents are a major national problem, each accident is local; prevention, therefore, must also be local. The role of the Public Health Service must be one of ascertaining facts, defining problems, developing techniques, devising methods applicable over broad areas of the Nation, disseminating information, providing expert consultation, stimulating the upgrading of professional competence, and encouraging State and local health officials to recognize and assume their responsibilities for effective action. The extent to which State and local health departments have begun to undertake broad accident prevention programs is gratifying proof of the value of Public Health Service activity in this field. A total of 24 State health departments now report participation in some traffic safety activity; 41 States report activities in some aspect of family safety. Two States employ full-time personnel in traffic safety; 12 States report full-time personnel in family safety.

Similarly, the increasing interest of qualified scientists in the pursuit of basic, applied, and developmental research problems related to accident prevention is, to a great extent, a result of Public Health Service encouragement. Perhaps the greatest contribution the Service will be able to make toward the eventual diminution of the accident problem will be in stimulating imaginative and painstaking scientists and engineers to develop for us basic information that is so badly needed, and to devise methods of anticipating and overcoming human failings that make such a great contribution to accidents. Public Health Service grants for accident prevention research increased from $83,000 in 1956 to $1,125,000 in 1960.

A third general area in which at least a beginning has been made is in training. There is a great need at all levels of Government for physicians, nurses, and other health personnel with specialized accident prevention training. At present, this type of training is not readily available. Recognized educational institutions are being encouraged to establish both long and short courses tailored to the requirements of Federal, State, and local and privately financed accident prevention programs. Assistance is rendered to such institutions through advisers, lecturers, and the provision of resource material. The Service is now working with schools of public health to improve and extend the teaching and accident prevention.

Another significant contribution has been made in the long-needed effort to coordinate the activities of a great number of agencies, both public and private, working in the field of accident prevention. Some of these are interested in the broad spectrum of the problem, others in isolated segments thereof. Some are national in scope; others have only regional or local interests. Nevertheless, all are accumulating valuable experience and knowledge. A real effort is being made toward the evaluation, amalgamation, exchange, and application of the experience and findings of these heterogeneous groups. Through this coordinated approach many needs are being identified and joint courses of action are being agreed upon. Participation in efforts to coordinate accident prevention activities has been the practice of the Public Health Service in the interest of good management and economy.

Under the heading of specific accomplishments are a number of pilot projects which have already paid off in a visible reduction in injuries and which will continue to benefit the Nation as their findings are applied in wider areas.

One of these is a project in one county of Arkansas to which two Public Health Service representatives were assigned on a full-time basis. Here, as in many other areas of the South, fires were a leading cause of death and disability. Epidemiological investigation revealed that improper wiring of homes and improper use of coal oil accounted for a substantial number of the accidental deaths and injuries. There has already been a dramatic reduction in the human and property losses from fires, as a result of educational and other corrective measures instituted in the county.

A review of the data on persons hospitalized because of accidents in the Shenandoah Valley area indicates a reduction in the first year of about 20 percent in the incident of injuries in the preschool child and young married adults. This would indicate that the family approach used was practical and can be applied in other rural areas.

A small pilot epidemiologic study of falls in elderly persons in Albany County, N.Y., suggested the hypothesis that broken hips from falls in elderly persons may in large part be due to a preexisting physical condition. This lead is being followed.

Following five regional conferences on the subject of drinking and driving, a national working conference on this subject will be held in May of 1961. An effort is being made to bring together all presently known facts on drinking drivers and pedestrians who have been associated with over 50 percent of vehicular deaths. These data will be assembled for use in developing and carrying out prevention programs.

A conference on simulation held February 27 through March 1, 1961, constituted the opening of a long-range effort to promote a better understanding of and the need for what may well be the most valuable single device ever developed in the campaign to reduce the death and injury rates on the Nation's highways through research. The form of the simulator has already been predicted in a feasibility study sponsored by the Public Health Service. Although many technical problems remain to be solved, these are now mainly of an engineering and developmental nature. When a simulator is built as the prototype of the several that are needed around the country, scientists will have a much more effective method for conducting research dealing with the many human factors that are involved in driving, without risking the lives of the drivers or others. The importance and value of this research device cannot be overestimated.

Prior to fiscal year 1961 major emphasis was directed toward the diagnosis and treatment of poisoning. Beginning in 1961, additional emphasis is being placed on the prevention of accidental poisoning. A pilot cooperative project to develop and test prevention measures and educational materials is being carried out in a local health department. Also, a medicine cabinet, developed by the Public Health Service, that is convenient for adult use but inoperable by small children is being considered by manufacturers for commercial production. prevention of the serious consequences of lead poisoning in children is being approached through the testing of various early detection, diagnostic methods to determine which is the most suitable for general screening use. The use of gastric lavage as treatment for accidental ingestions of kerosene has been evaluated. On the basis of these recent research efforts, it can be concluded that gastric lavage does not encourage the development of pulmonary complications as had been believed. There is indication that such treatment results in a reduction of pulmonary complications.

This, of course, can be only a quick sampling of the many avenues of accident prevention being explored by the Public Health Service and being exploited as rapidly and as thoroughly as available funds and manpower allow. The types of activities which, by research and application, can significantly reduce the accident toll in the future include, among others, encouragement of general proficiency in mouth-to-mouth resuscitation, improvement of safety standards for household appliances, epidemiological studies of motor-vehicle deaths to identify preventable causative factors, and the development of criteria to determine who is capable of safely operating motor vehicles under modern traffic conditions.

Research grant funds

In the area of accident prevention, 29 research grants were supported in 1960. In 1961, continuing studies and new grants are expected to bring the total amount to $1,482,000. The grants in these 2 years supported research at 14 universities, 4 State health departments, and 9 independent research organizations. These studies are all aimed at a reduction of the threat of accidents to public health—accidents, on the highway, in the home, at work and at play—accidents which are responsible for an annual toll of more than 90,000 deaths and over 9 million disabling injuries. Some representative problems under study are:

Crash injuries in automobiles and aircraft.
Accidental poisoning.
Driving behavior and accidents.
Safety devices in cars.
Childhood accidents.
Adolescent driver characteristics.
Driver education.
School-age accidents and education.

It is anticipated that such research will uncover some of the basic causes of accidents and will permit the development of effective preventive measures.

ACTIVITIES UNDER THE GRANT TO THE INTERNATIONAL ASSOCIATION OF CHIEFS OF POLICE

The chief investigator, Mr. Robert Shumate, reports that even though it has been less than a year since the start of work under this grant, progress has been substantial, and two technical papers are in manuscript. An instrument has been developed which is actuated by an invisible tube on the highway and photographs each car going by and its location on the highway, and records its speed and the time. This information is recorded at the beginning and end of a sample segment of road, for each vehicle passing through. The information is fed into an IBM 650 computer through special programing developed under this grant. Out of it comes a continuous record of the traffic in this segment of road, including such phenomena as passing time, passing, headway, the formation of queues, and in short, the behavior of the entire traffic column.

The accident experience of the entire Wisconsin State road system for 3 years has been broken down into about 2,000 segments. A number of segments have been analyzed and the accident experience on them found to be consistent from year to year. Work is in progress in relating the accident experience in each segment of road to the traffic patterns as determined by the computer analysis. After this phase is completed, the investigators will attempt to develop enforcement patterns which will systematically change hazardous traffic patterns which tend to form on certain segments of the highways.

PROSPECTS FOR THE FUTURE

The action of Congress last year in appropriating additional funds for accident prevention work has had a salutary effect on the national effort in this field. More researchers are entering the field, more facets of the problem are being studied, and more vigorous action programs are being carried out. These efforts, however, will require additional encouragement and practical support before any lasting and measurable acceleration of the downward trends in accidental deaths and injuries can reasonably be expected. There is no doubt that a concentrated effort at identifying and correcting, eliminating, and compensating for the human failing which causes accidents will accelerate this downward trend. Emphasis must continue to be directed toward traffic, home, farm, and recreation accidents.

The economic losses due to accidental deaths and injuries, the human suffering entailed, and the tragic loss of lives among our youngest and potentially most productive citizens, all emphasize the need for constructive, preventive action, much of which is peculiarly within the experience and capabilities of the Public Health Service.

Under the new concept that "accidents don't happen; they are caused," public health agencies and all of the health professions are focusing their technical know-how and their humanitarian instincts on the solution of those accident problems which come within their professional purviews. Their efforts have already begun to make an impact on the accidental death and injury problem. What is more important is that they are beginning to identify additional areas that are amenable to public health treatment and to devise specific remedies for specific types of accident hazards.

Every new fact which is uncovered, in addition to providing new knowledge that can be brought to bear against accidents, serves also to increase our awareness of the vast amount of knowledge that is still needed and to point to new and important research that must be performed if the present high incidence of accidents is to be significantly reduced. The potential value of such research and the new information it will provide is evident in the figures cited above.

AMENDMENT TO THE 1962 BUDGET

Budget page	Heading	Original estimate	Revised estimate	Increase
640	Community health activities	$61,750,000	$63,750,000	$2,000,000

Program and financing

[In thousands]

	1962 original estimate	1962 revised estimate	1962 increase
Program by activities:			
1. Grants to States for general health	$17,820	$17,820	
2. Grants for public health training	5,000	5,000	
3. Accident prevention	3,368	3,368	
4. Chronic diseases and aging	1,998	3,958	$1,960
5. Communicable disease activities:			
(*a*) Communicable Disease Center	9,271	9,271	
(*b*) Control of venereal diseases:			
1. Grants to States	2,400	2,400	
2. Direct operations	3,415	3,415	
(*c*) Control of tuberculosis:			
1. Grants to States	4,000	4,000	
2. Direct operations	2,493	2,493	
(*d*) Arctic Health Research Center	508	508	
6. Community health practice and research	1,961	1,961	
7. Dental services and resources	2,182	2,182	
8. Nursing services and resources:			
(*a*) Training grants	6,525	6,525	
(*b*) Direct operations	810	850	40
Total program costs	61,750	63,750	2,000
Financing: Appropriation (new obligational authority)	61,750	63,750	2,000

Object classification

[In thousands]

	1962 original estimate	1962 revised estimate	1962 increase
01 Personal services:			
Permanent positions	$13,029	$13,250	$221
Positions other than permanent	1,686	2,935	1,249
Other personnel compensation	118	118	
Total personnel compensation	14,833	16,303	1,470
12 Personnel benefits	1,795	1,866	71
21 Travel and transportation of persons	1,406	1,497	91
22 Transportation of things	261	268	7
23 Rent, communications, and utilities	344	344	
24 Printing and reproduction	222	265	43
25 Other services	735	735	
Research contracts	1,242	1,542	300
Payment to “Bureau of State Services management fund”	2,618	2,618	
Payment to “National Institutes of Health management fund”	25	25	
26 Supplies and materials	1,001	1,006	5
31 Equipment	525	538	13
41 Grants, subsidies, and contributions	36,745	36,745	
Subtotal	61,751	63,751	2,000
Deduct quarters and subsistence charges	−1	−1	
Total obligations	61,750	63,750	2,000

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	2,020	2,149	2,324
Full-time equivalent of other positions	208	269	665
Average number of all employees	1,995	2,182	2,745
Number of employees at end of year	2,122	2,393	2,903
Average GS grade	6.9	7.0	7.0
Average GS salary	$5,705	$6,102	$6,073

COMMUNITY HEALTH ACTIVITIES, PUBLIC HEALTH SERVICE

JUSTIFICATION

This amendment of $2 million in the community health activities appropriation will provide for the expansion of community health services in the chronic disease and health of the aged program and the establishment of an advisory committee on nursing education and nursing services during fiscal year 1962.

Chronic diseases and aging

The White House Conference on Aging dramatically and forcefully reemphasized the growing concern of State and community leaders over health and medical care problems of our aging population. Proposals submitted to the Conference by individual States show a remarkable consensus and point unmistakably to the lack of community health services for older people as the most significant health problem facing communities today. Among 46 States, 36 submitted recommendations for home nursing services, 26 for organized home care programs, 31 for homemaker services programs, 36 for restorative services, 18 for information and referral, 16 for outpatient geriatric clinics and 32 for raising the standards of care in nursing homes. The impact of the Medical Assistance Act, the White House Conference on Aging, and the individual State conferences which preceded the White House Conference, have created an atmosphere of community interest and awareness in this important community health problem that is without precedent. Possible legislative changes in prospect which may provide new methods of payment for medical care can only serve to increase an already strong demand for establishing community services where they do not now exist. Many States, because of legislative changes required and for other reasons, have delayed activation of their broad medical assistance programs authorized under the provisions of the Medical Assistance Act. By 1963, however, it is predicted that many of these States will be embarking on full-scale programs with a resultant demand for establishing home health programs. Pending possible legislative changes which may broaden this important program, it is estimated that fiscal year 1963 will be the first effective year of operation of any altered or broadened plan.

It is, therefore, important and urgent that we move forward immediately to assist health agencies in solving the problems of organization, initial financing, training and in the administration of such home service programs. To many communities, this is a new responsibility and one which most of them are not well prepared to meet without our assistance. Unless these services can be developed, medical assistance funds will be utilized for providing higher priced institutional care services with the result that fewer old people will benefit. Our working experience over the last few years has shown that the provision of funds for defraying part of the initial cost for a period of 1 to 4 years is a most effective means of insuring the development of permanent and continuing activities. Consideration must also be given to the fact that there has been no other single source of funds except general health formula grants available from the Public Health Service which could be utilized for this broad purpose.

The extreme urgency of this request is such that it is planned to use existing authority to negotiate cooperative projects for new program development which is the most effective method of stimulating community action on a widespread basis that is now available to this program. In addition, study is being given to the matter of finding more effective ways and means of providing the impetus and stimulation required for the early development of community health services in this field. However, in the meantime, we would make a beginning in 1962 by offering cooperative assistance to approximately 75 communities where these services are nonexistent or not well organized to develop new programs. These new programs include home nursing care, coordinated home care, homemaker services, information and referral programs, periodic health appraisals and programs for raising the standards of care in nursing homes. For carrying out this accelerated program an increase of $1,960,000 and 42 positions is requested.

The major portion of these funds will be used in those specific program areas which have as their focus the care of the chronically ill and aged in their own homes. Of the total amount $250,000 will be used for developing new information and referral programs, an activity which has had proven community usage as a method of pointing up health services shortcomings and which can also serve as the initial focus for bringing together existing services within the community. Information and referral programs are relatively simple to start and can be the stimulus for the more extensive development of comprehensive programs for the chronically ill and aged. Some of the increase, $225,000, would be utilized to augment our nursing home program which was initiated last year. Real progress is being made in this area and the additional funds and positions requested will enable us to step up our rate of progress significantly.

A small proportion of the increase will be utilized for studies and demonstrations of periodic health appraisals. The value of periodic health examinations has long been recognized as a most effective method of detecting disease and illness early, but much remains to be done to establish uniform testing procedures to be recommended for the various age groups and in developing new programs as a community health activity. We propose to expand our initial effort in this area with the increase of $100,000 requested.

It is recognized that the previous submission did not utilize the full potential of new State and community interests and awareness in this field which was brought to the fore by the White House Conference. Using existing authorizations this amended budget request would permit us to make a beginning in the development of a vigorous program designed to assure that these urgently needed health services for the aged and chronically ill are available where and when they are needed. The lack of these services in the average community, and the growing consumer demands for establishing programs for the care of the sick at home attest to the urgency of this request for increased funds to enable the Public Health Service to fulfill, at least in part, its obligations in this important health program development.

Nursing services and resources

An advisory committee on nursing education and nursing services will be established to produce the data and recommendations through which the Public

Health Service can take a position and make appropriate proposals to assure an adequate quantity and quality of nurses for the future. January 1, 1962, is the target date to have available the findings of this advisory group.

The committee will view the current and foreseeable needs for nursing services including—

1. The need for Federal aid for construction of educational facilities, and for what types of educational institutions.
2. The need for Federal aid to assist in meeting educational costs, and for what types of institutions.
3. The need for scholarships from Federal funds for students in basic professional education and for what types of programs as well as the problem of continuation of scholarships for graduates in general and specific fields.

The committee will recommend those actions which will best assure that these needs are met in an optimal fashion. It will also recommend which of those actions, if any, the Federal Government should take.

An increase of $40,000 will provide funds for travel and related costs for meetings of this group.

Monday, March 20, 1961.

HOSPITAL CONSTRUCTION ACTIVITIES

WITNESSES

DR. JACK C. HALDEMAN, CHIEF, HOSPITAL AND MEDICAL FACILITIES

ACCOMPANIED BY:

DR. LUTHER L. TERRY, SURGEON GENERAL

HARRY L. DORAN, CHIEF FINANCE OFFICER

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	1,376	1,520	1,559
	Positions other than permanent	28	27	27
	Other personnel compensation	10	6	------------
	Total personnel compensation	1,414	1,553	1,586
12	Personnel benefits	83	100	100
21	Travel and transportation of persons	136	135	135
22	Transportation of things	10	6	6
23	Rent, communications, and utilities	15	14	14
24	Printing and reproduction	22	19	19
25	Other services	33	32	32
	Payment to "Bureau of State Services management fund"	52	56	59
26	Supplies and materials	13	11	11
31	Equipment	13	10	10
33	Investments and loans	2,000	450	500
41	Grants, subsidies, and contributions	152,274	188,100	170,000
	Total obligations	156,065	190,486	172,472

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	194	196	196
Full-time equivalent of other positions	4	4	4
Average number of all employees	178	180	185
Number of employees at end of year	181	191	200
Average GS grade	8.8	9.2	9.2
Average GS salary	$7,280	$8,069	$8,069

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(a) Construction of hospitals, etc., under part C of the Public Health Service Act	125,016	151,941	134,500
(b) Construction of medical facilities under part G of the act:			
(1) Chronic disease hospitals	3,693	6,091	9,000
(2) Diagnostic or treatment centers	6,747	7,593	7,500
(3) Rehabilitation facilities	7,994	10,183	8,500
(4) Nursing homes	9,812	11,742	10,000
Total construction grants	153,262	187,550	169,500
2. Hospital and medical facilities research	1,190	1,200	1,200
3. Operations and technical services	1,604	1,736	1,772
Total program costs	156,056	190,486	172,472
4. Relation of costs to obligations: Obligations incurred for costs of other years, net	9		
Total obligations	156,065	190,486	172,472
Financing:			
Comparative transfers from (−) other accounts	−1,612	−1,736	
Unobligated balance brought forward	−95,726	−127,051	−124,500
Recovery of prior year obligations	−13		
Unobligated balance carried forward	127,051	124,500	105,000
Unobligated balance lapsing	436		
New obligational authority (appropriation)	186,200	186,200	152,972

Mr. FOGARTY. Dr. Haldeman, Mr. Denton may have to leave before you get through, and he has some questions he would like to ask you.

Dr. HALDEMAN. Yes, sir.

DIFFICULTIES IN AREAS WITH INSUFFICIENT MEDICAL AND HOSPITAL FACILITIES

Mr. DENTON. You were here when I asked what could be done in counties that do not have doctors, were you not?

Dr. HALDEMAN. No, sir; I was not.

Mr. DENTON. I spoke about one county in the district I represent which has only one doctor, no dentist. Of course, if we had a hospital there we would have little difficultly in getting doctors, but I do not think that the county is financially able to pay their share of building a hospital. Do you have any suggestion as to what could be done about this situation?

Dr. HALDEMAN. Actually the problem of a small community that has only one physician is a difficult one. The problem is not so much of providing a facility for him to work in, that is, office space and laboratory space, but rather it is one of getting a physician to come to the community. The Sears, Roebuck Foundation has had perhaps the most experience in this area.

Mr. DENTON. We have been working on that.

Dr. HALDEMAN. As you perhaps know, they do a survey of the community to determine whether the community can economically afford to have a physician. Their experience has been that the community is able to raise the funds to construct office and laboratory space for them if they can get the physician. They have had a very good record with communities that they have gone in to help. They are helping through loans to get the physician in there and perhaps subsidize his income for a year or two to get him going.

Mr. DENTON. Who subsidizes his income Sears, Roebuck or the county?

Dr. HALDEMAN. Sears, Roebuck will loan the money to assist in getting the physician there. They do not loan money for facilities. If the sponsor is a governmental agency or a hospital, a diagnostic and treatment center can be built with Federal aid under the Hill-Burton Act; but I think a small community wanting a physician had better look into the situation pretty closely to make sure that it can support a physician and a medical facility. Sometimes it is better to travel a little distance to where there is a more adequate facility. Medicine is getting so complicated today that it is very difficult to practice scientific medicine unless you are close to a hospital.

Mr. DENTON. It is difficult to make a trip of 40 or 50 miles to get a doctor or a dentist.

Dr. HALDEMAN. Well, if it is that far to a doctor or a dentist it would probably warrant having them in the area.

Mr. DENTON. Another difficulty we have is that the Government and State own a big share of the land in that county.

That is all. Thank you.

Mr. FOGARTY. Doctor, do you have a statement for the committee?

Dr. HALDEMAN. I will be very happy to read a short statement.

Mr. FOGARTY. All right. Go ahead.

GENERAL STATEMENT

Dr. HALDEMAN. Mr. Chairman and members of the committee, the purpose of the Hill-Burton program is to assist the States in providing more adequate hospital and medical facility services to the people. Our request for 1962 is $187,972,000. This amount will provide $125 million for the construction of hospitals and public health centers, $60 million for the construction of long-term ambulatory and rehabilitation facilities. It will also provide $1,200,000 for research and demonstration activities, and $1,772,000 for operations and technical services.

The $185 million requested for construction purposes will enable the States to start the construction of 761 health facility projects, involving 25,213 hospital and nursing home beds and 294 units for various types of outpatient care.

Since the Hill-Burton program was initiated substantial progress has been made in the construction of general hospital beds and facilities particularly in rural areas. However, the same substantial progress has not been made in the construction of long-term care facilities and facilities for care and treatment of ambulatory patients. For this reason, the full amounts authorized to be appropriated for nursing homes, chronic disease hospitals, diagnostic or treatment centers, and rehabilitation facilities have been included in our request.

As of December 31, 1960, approximately $1.4 billion had been committed to 5,390 projects costing a total of almost $4.7 billion. Completion of these projects will add 226,842 hospital and nursing home beds and will result in the construction, expansion, or remodeling of 1,496 public health facilities, diagnostic or treatment centers, and rehabilitation facilities. While less dramatic, the other Hill-Burton accomplishments are probably of equal importance. For example: the program has resulted in a better distribution of facilities throughout the country, has upgraded the quality of medical care provided in rural areas, and has exerted a tremendous influence on the design and construction of hospital facilities both in this country and abroad.

The funds requested for construction grants are in the same amount as was appropriated last year. However, the distribution of the total among the various categories of facilities has been changed so as to begin the correction of imbalances which exist in the availability of general hospital beds as opposed to facilities for long-term and ambulatory care.

An amount of $1,200,000 is also included in this request for the purpose of carrying out research activities relating to hospital facilities, resources, and services. It is believed that the best hope for putting a damper on spiraling hospital costs lies in the systematic study of each area of hospital operation, and the application of the results of research to the development of more efficient organizational patterns for the provision of health services, better techniques of administration, improved design of the physical plant, and better coordination of community health facilities and resources.

Finally, a request is made for $1,772,000 for salaries and expenses necessary to operate the Hill-Burton program. No additional positions are included in the request.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

(Dr. Haldeman's full statement was supplied for the record as follows:)

STATEMENT BY CHIEF, DIVISION OF HOSPITAL AND MEDICAL FACILITIES

Mr. Chairman and members of the committee, the purpose of the Hill-Burton program is to assist the States in providing adequate hospital and medical facility services to the people. The basic methods used in operation of the program have not changed. First, State agencies must develop a comprehensive plan designed to meet the hospital and medical facilities needs of the States; secondly, construction projects are approved in the order of priority; and thirdly, research and experimental studies and demonstration projects are carried out as a means of developing new organizational patterns of providing hospital services and improving the operation, utilization, and design of health facilities.

1962 ESTIMATE

The original budget for hospital and medical facilities construction, for research activities, and for salaries and expenses requested $152,972,000. The revised budget requests $187,972,000 which will provide $125 million for construction of hospitals and public health centers; $60 million for construction of nursing homes, diagnostic or treatment centers, rehabilitation facilities, and chronic disease hospitals; $1,200,000 for research, experimentation, and demonstrations; and $1,772,000 for operations and technical services.

PROPOSED PROGRAM FOR 1962

Construction

The $185 million requested for construction purposes will enable the States to start the construction of 761 health facility projects involving 25,213 hospital and nursing home beds and 294 units for various types of outpatient care. This projection is based on the assumption that State agencies will program the construction of the different kinds of health facilities during 1962 along the same lines as construction was programed during 1957 and 1958.

Substantial progress has been made in the construction of general hospital beds and facilities in rural areas. In 1948 only 59 percent of the general hospital beds needed were in existence, whereas State agencies reported on January 1, 1960, that 79 percent of the general beds needed were available. That portion of the construction funds requested, which previous experience indicates will be devoted to production of general beds, plus those funds used for this purpose outside the program will produce 31,977 general beds. This number is sufficient to offset the general beds needed because of population increases and those which will become obsolete during the year. In addition, the deficit of general hospital beds will be decreased by 6,480.

However, the same substantial progress has not been made in the construction of other health facilities, such as long-term care, rehabilitation, and outpatient facilities. For this reason, the full amounts authorized to be appropriated for nursing homes, chronic disease hospitals, diagnostic or treatment centers and rehabilitation facilities are included in the revised budget for the purpose of beginning the correction of the imbalances existing among the various kinds of facilities.

Research

The amount of $1,200,000 requested for research activities is the same as was appropriated for 1961. Continued research, experimentation, and demonstration relating to hospital services, facilities, and resources are necessary if the physical plant, equipment, and organizational and operational aspects of our health facilities are to reach peak efficiency. While such research is not the only answer to the financial crisis facing hospitals today, it is believed that it represents our best hope for developing improvements in hospital organization, operation, and design which will help to put a damper on the spiraling costs of hospital care.

The concept of progressive patient care, which we have been pushing under this program, is rapidly being accepted as an improvement in hospital organization. Many hospitals have already adopted one or more elements of the progressive patient care concept, and many others have plans to do so. While additional research remains to be done in the field of progressive patient care, it gives promise of improving the utilization of scarce professional skills and at the same time improving the quality of patient care.

FACILITIES AND BEDS CONSTRUCTED UNDER THE HILL-BURTON PROGRAM

As of December 31, 1960, approximately $1.4 billion in Federal funds had been committed to 5,390 projects costing a total of almost $4.7 billion. Of these projects, 3,765 have been completed, are in operation, and are serving their communities; 1,341 are under construction, and the remaining 284 are in the preconstruction stages. Completion of these projects will add 226,842 hospital and nursing home beds, and will result in the construction, expansion, or remodeling of 966 public health facilities, 365 diagnostic or treatment centers, and 165 rehabilitation facilities.

HIGHLIGHTS OF ACTIVITIES DURING THE PAST YEAR

While the program has continued to move ahead in providing assistance in the construction of facilities, we are at the same time reevaluating the existing program and making plans for the future. Health facility planning must keep pace with the latest developments in medicine and the socioeconomic trends of our times. In order to update the planning techniques used in the program, we have been instrumental in establishing several ad hoc committees for the purpose of developing guidelines and principles in specific areas of health facility planning. The findings and reports of these committees should have a pronounced impact on the future hospital plant of our country, and for this reason a brief description of each committee and its function may be helpful and of interest to you.

1. *Areawide Health Facility Planning Committee.*—This committee, jointly sponsored by the Public Health Service and the American Hospital Association, and chaired by Mr. George Bugbee, has developed a general approach to the future planning of hospital and other medical facilities in densely populated areas. Special recognition is being given to problems stemming from the growing obsolescence of older institutions, and the complex problems involved in the more urban areas of our country.

2. *Mental Health Committee.*—This committee, composed of representatives of Hill-Burton State agencies, State mental health authorities, and the Public Health Service is developing principles and guidelines for constructing mental health facilities to conform with modern concepts of treatment and care. Forma-

tion of the committee was the outgrowth of increasing recognition of (a) the magnitude and importance of the problems of mental illness, and (b) the need for a comprehensive program stressing continuity of care which requires a wide spectrum of services both community based and hospital oriented. The report of the committee has been published.

3. *Tuberculosis Facilities Committee.*—The purpose of this committee is (a) to analyze and review data on the incidence and prevalence of tuberculosis and the recent trends in the use of tuberculosis beds in order to determine the future need for these facilities, and (b) to develop principles to guide States and communities in the construction of new facilities and the conversion of existing facilities no longer needed for the treatment of the tuberculosis patients. Joint sponsors of this project are the Public Health Service and the National Tuberculosis Association.

4. *Vocational Rehabilitation Facilities Committee.*—The Division, in cooperation with the Office of Vocational Rehabilitation, has established a committee to develop better principles and guidelines to be used by Hill-Burton State agencies and other planning groups in developing plans for adequate rehabilitation facilities and services. Material used by the committee as a basis for its recommendations includes the findings of a staff study of rehabilitation centers of the various types constructed under the Hill-Burton program since 1954. A reevaluation of the planning principles and guidelines now being used by State agencies will be included in the study.

Serious consideration is being given to establishment of an ad hoc committee for planning long-term care facilities and services. The possibility of enactment of Federal legislation, which would partially remove the present financial barriers to care in long-term facilities, makes it imperative that we reevaluate our present planning principles and develop guidelines to assist us in meeting the challenge which is facing us.

OPERATIONS AND TECHNICAL SERVICES

The amount of $1,772,000 is requested for salaries and expenses incident to carrying out the program. No additional positions are requested for 1962.

The professional and technical staff supported by the funds requested consist of medical officers, public health specialists, architects, engineers, and equipment specialists in the regional and central offices. They represent the nucleus of of the basic staff required to administer the program, and are responsible for the continued leadership of the Federal Government in the field of health facility planning, design, and construction.

Explanation of need

Several of the most important activities supported by the funds requested are as follows:

1. The development of minimum standards of design, construction, and equipment is a continuous activity and one which has contributed much to the success of the program. These standards must be revised continuously if new health facilities are to keep pace with the rapid and dramatic changes occurring in the practice of medicine. The guide material developed as a result of this activity is used extensively by States and communities in planning and constructing facilities, and gives maximum assurance that Federal dollars will produce well planned and well constructed facilities.

2. The review, analysis, and approval of State plans represent one of the most important aspects of program operation. The State plan document includes the State agency's analysis of the need for additional hospital and medical facilities within the State, identifies the communities in which new or expanded facilities should be constructed, and establishes an objective system of priorities which is used as the basis for selection of projects to receive aid. Extensive technical assistance is given State agencies in the development of State plans and significant amounts of staff time are devoted to their review, analysis, and approval since this document establishes the basic framework for each State's program during the fiscal year.

3. The development and interpretation of regulations, procedures, and policies establishes a comprehensive administrative framework within which State agencies carry out their responsibilities for program operation. This activity also enables the Public Health Service to make important delegations of authority to our regional offices. While legislative requirements and sound principles of administration must be a part of all regulatory material, the varying staff

and different methods of operation employed by the 50 States, the District of Columbia, Guam, Puerto Rico, and the Virgin Islands require that maximum flexibility be injected into all operating policies and procedures.

4. Basic documents, such as project applications, including architectural drawings and specifications, must be reviewed and approved. In addition, projects under construction must be inspected, requests for Federal funds must be certified for payment, and surveillance must be maintained over bid and award procedures. These activities are essential elements of the operating program, and the speed and thoroughness with which they are carried out are important to the success of the program.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

THE 1962 BUDGET REQUEST

Mr. Fogarty. What did you ask the Bureau of the Budget for, Doctor? Or, first, what did you ask the Department for?

Dr. Haldeman. The Public Health Service requested $178,294,000.

Mr. Fogarty. And now you have a revised budget of $187 million?

Dr. Haldeman. The present revised budget is $187,972,000.

Mr. Fogarty. What did you ask for, your full authorization; $211 million?

Dr. Haldeman. $211.2 million for grants and research, and $2,094,000 for operations and technical services, or a total of $213,294,000.

Mr. Fogarty. Where did it get cut? At the Department or the Bureau of the Budget?

Dr. Haldeman. The request for grants was reduced in the Office of the Surgeon General to the $185 million figure. The reduction of $322,000 in operations and technical services was in the Bureau of the Budget.

CRITERION FOR BUDGET AMENDMENTS

Mr. Fogarty. We were told that the Food and Drug Administration budget amendment was turned down because it failed to meet the President's criterion that an amendment must represent "a significant change in the scope or direction of Government programs." What is the difference between their requested increase and this one in that regard?

Mr. Kelly. The fact that the Eisenhower budget expected a reduction below the current level of the program. It is a determination of the new administration that they do not want such a reduction to occur, and it is quite a substantial increase.

Mr. Fogarty. Does that happen in any other place—where you just increased it because the Eisenhower budget was less?

Mr. Kelly. I think under existing legislation this was the only item that had any major reduction below the current level, and it was the decision to reinstate that reduction.

SHIFT IN EMPHASIS

Mr. Fogarty. I see. The total is the same as the 1961 appropriation, but the breakdown is somewhat different in that there is a cut of $25 million in the general hospital section and an increase of $25 million for the other categories.

Dr. Haldeman. That is correct.

Mr. Fogarty. Was this your decision?

Dr. HALDEMAN. Yes. I was primarily responsible for this. The distribution of funds was made in this fashion, in order to give greater emphasis, or, rather, to get a better balance between the various types of facilities. We have made a lot of progress in the general hospital category, although we have ground to make up there too; but at the beginning of the program——

Mr. FOGARTY. Well, you have a lot of ground to make up.

Dr. HALDEMAN. In this category at the beginning of the Hill-Burton program there was only 59 percent of the beds needed in the general hospital category, and now there is 80 percent. We have not made the same progress in long-term and ambulatory care. We are much further behind in the construction of these types of facilities which would cut down on the need for general hospital beds, and hopefully reduce the costs of providing services. There are a great many patients in the general short-term hospitals who could be better cared for in skilled nursing homes under medical supervision if we had suitable homes for them to go to.

So I think this is a direction in which we are going to have to go if we are to put a damper on spiraling hospital costs.

Mr. FOGARTY. Is this one way of getting hospital costs down, do you think?

Dr. HALDEMAN. Oh, definitely. I feel that putting the right patient in the right facility, the development of ambulatory care facilities and outpatient departments as well as hospital and community-based home nursing programs will all have the effect of reducing the need for inpatient care or general hospitals.

FACTORS AFFECTING HOSPITAL POPULATION AND COSTS

Mr. FOGARTY. Do these insurance plans like Blue Cross and Blue Shield have any effect on the population in the hospitals?

Dr. HALDEMAN. Yes, they do have an effect on it. I do not think the effect is as great as is sometimes thought, but I am sure that some patients are admitted to the hospital for diagnostic procedures because Blue Cross will pay for that admission but will not pay for diagnostic procedures administered on an ambulatory basis. However, there have been studies made that show if diagnostic services are included as a Blue Cross benefit that the result is an increase in hospital utilization. This is contrary to what many of us have been saying for years. What happens is people use the diagnostic facility more, consequently more conditions requiring hospitalization are discovered, and the total amount of hospitalization increases.

Mr. FOGARTY. Let us talk about some of the studies in this field.

Dr. HALDEMAN. There is a study by Max Shain entitled "The Epidemiological Approach to Hospital Utilization." The basis for the findings in this study is a physician review of 953 consecutive records from three medium-sized general hospitals in central New York State. As a result of this review it was reported that about 4 percent of the admissions were classified as questionable, which meant that both the diagnostic and treatment services were characterized as procedures that could easily have been done outside the hospital, or that no significant procedures were performed. There were significantly high proportions of questionable admissions among men between 15 and 24 and women over 65. Five percent of the total number of patients were judged to have been in the hospital for periods that were probably or definitely excessive.

In a study by Ray Trussell a review was made of 651 patient records in five hospitals in New York. This study found that 87 percent of the admissions appeared to be medically necessary. Eight percent of the admissions seemingly were not required on a medical basis. The study recommended that there should be an increase in ambulatory services and diagnostic services and that every hospital should have a utilization committee, which many hospitals do have.

Mr. FOGARTY. Put the complete statements on a few of those in the record, Doctor.

Dr. HALDEMAN. I will be glad to.

(The statements concerning these and other studies follow:)

SHAIN

Shain, Max, "An Epidemiological Approach to Hospital Utilization," Hospital Management 90:50–51, 113, October 1960.

The basis for the findings in this article is physician review of 953 consecutive records from three medium size general hospitals in central New York State for the month of February 1957.

As a result of this review, it was reported that about four percent of the admissions were classified as "questionable," which meant that both the diagnostic and treatment services were characterized as procedures that could easily have been done outside the hospital or that no significant procedures were performed. There were significantly high proportions of questionable admissions among men between 15 and 24 and women over 65. The two diagnostic groups which were signally high among the questionable admissions were arthritis and rheumatism and accidents.

Five percent of the total number of patients were judged to have been in the hospital for periods which were probably or definitely excessive. It was believed that many of these patients might have received at least part of their care outside of an acute general hospital—some through home care programs, others in nursing homes or chronic disease hospitals. It was realized that these latter types of facilities are not plentiful in small communities.

TRUSSELL AND VAN DYKE

Trussell, Ray E., M.D., van Dyke, Frank, "Prepayment for Hospital Care in York State," New York, Columbia University School of Public Health and Administrative Medicine, 383 pages.

The authors state the projection of trends during the 10-year span 1947–57 indicates that hospital costs will increase at least 50 percent by 1967. For this reason, efficient hospital utilization becomes increasingly important.

They list the three costly components of utilization as:

1. The fact of admission.
2. The services provided during hospitalization.
3. The length of stay.

To evaluate the need for hospital admission, 651 patient records in five hospitals were reviewed. It was found that 87 percent of the admissions appeared to be medically necessary. Eight percent of the admissions seemingly were not required on a medical basis, while for 5 percent it was not possible to form an opinion based on the information on the record. Therefore, it was concluded, it would appear from the results of the evaluation that in approximately one of every eight admissions, the necessity of that admission would require staff committee review.

The authors found no evidence that utilization of ancillary services by Blue Cross patients was excessive, when based on comparison of Blue Cross use of these services with that of patients with a comprehensive type of commercial insurance coverage.

The authors point out that unnecessary length of stay by hospital plan members constitutes a form of exploitation of all other members, as it increases the cost of the insurance payment. It also adds to the total community cost of medical care by increasing the construction costs necessary to provide facilities, since, if more people can be cared for in a year in a certain size hospital, the necessity for that expansion is lessened. Studies concerning length of stay in regard to the day of the week of admission and by other factors are included. It was found that there are wide variations in length of stay in different hospitals for patients with the same problems.

Among the recommendations made to effect more economical utilization are:

1. Ambulatory services, such as X-ray and laboratory tests, should be encouraged to minimize inpatient admissions.
2. Every hospital should have a utilization committee to study matter pertaining to admissions, use of services, length of stay, and standards of care.

ANDERSON AND FELDMAN

Anderson, Odin W., Ph.D. and Feldman, Jacob J. "Family Medical Costs and Voluntary Health Insurance: A Nationwide Survey," McGraw-Hill Book Co., Inc., 1956, 251 pages.

The authors conducted a survey in July 1953, based on single interviews of 2,809 families in their homes, representing a national sample of the population. They state that the survey was limited to an analysis of the financial aspects of personal health services, and that the purpose of the survey was to learn what effects the present range of benefits offered by voluntary insurance have on the increasing costs of personal health services and on the utilization of services.

Among the findings reported by the authors concerning hospital utilization are:

The general hospital-admission rate for the country as a whole was 12 per 100 population per year. The admission rate for persons with hospital insurance was 14, and for those without such insurance 9.

For the general population, including both insured and uninsured persons, the hospital-admission rate varies very little between different income groups. In fact, the highest-income group shows indications of having a lower admission rate than other income groups.

Hospital-admission rates in urban and rural areas have reversed themselves during the past 20 years, so that now rural areas have a higher admission rate than urban areas.

The mean length of stay for all hospital admissions was 7.4 days per person. Persons with insurance had a shorter length of stay than those without insurance, 7 and 8.3 days, respectively.

In the general population there were 90 hospital days utilized per 100 persons. The rate for persons with insurance was 100, and for those without insurance, 70. Apparently the increase in hospital days among the insured is attributable to increased female utilization, since insured and uninsured males both have a utilization rate of 70 days per 100 persons, and insured and uninsured females have a rate of 120 and 80 days per 100 persons respectively.

The number of hospital days per 100 persons by family income shows no consistent relationship for the general population. Among insured families, however, the lower the income the greater is the number of days utilized. Among families without insurance the higher the income, the greater is the number of hospital days utilized, with the apparent exception of the lowest income group.

KELLY

Kelly, Derwood N., "Experience With an Out-of-Hospital Diagnostic Program," Maryland State Medical Journal 8:80, February 1959.

The following is a report of the Hospital Planning Abstract Service, the American Hospital Association:

"This reports the results of a study in Maryland on what happened to hospital utilization rates of subscribers whose Blue Shield policies were liberalized to pay for certain diagnostic procedures done either at the hospital or at physicians' offices. The writer states that it has been claimed that providing such benefits to persons without requiring them to be hospitalized would reduce hospital utilization and thus to some degree offset the additional costs of the services provided.

"A group of about 123,000 persons, employees of a large heavy industry, had their regular Blue Cross-Blue Shield coverage augmented by a rider which would pay up to $75 per person in any 12-month period for diagnostic X-rays, electroencephalograms, electrocardiograms, and basal metabolic rates, done either in physicians' offices or at the hospital. There was no limit to payment for such services received in the hospital, either inpatient or outpatient.

"This study compares experience for the year immediately before and the two after the date of the new program. The writer uses three measurements of utilization: (1) Inpatient admissions per year per 1,000 subscribers, (2) average length of stay per admission, and (3) average number of days of care used per 1,000 subscribers per year. During the first year (old program) inpatient admissions per 1,000 subscribers were 97; during the second year the rate was 103, and in the third it was 107 (both years under the new program). Average length of stay varied from 7.69 days per admission to 7.58 to 7.92 during the 3 years studied. Days of care per 1,000 subscribers rose from 749 the first year to 784 and 850 the second and third years.

"The author concludes that this change has not been associated with a decline in hospital admissions but with the reverse. He points out that the utilization of the new benefit itself has risen. In the first year it could be used, the rate was 70 per 1,000 subscribers with an average cost of $18.65, but during the second year the rate increased 58 percent to 111 per 1,000, while the unit cost decreased only to $18.11. Total cost of services to nonhospitalized patients was $161,377 the first year and $246,684 the second. Diagnostic X-rays accounted for 77 percent of this expense; 83 percent of these tests were done in physicians' offices.

"The author stresses he is not against providing prepaid coverage for such outpatient or nonhospital services. They should not be provided under a belief that the cost will be offset by a saving on inpatient care. While these benefits should and will be used heavily, he concludes, they will materially increase the total premium cost of prepaid care."

ROOMER

Roomer, Milton I., M.D., "The Influence of Prepaid Physician's Service on Hospital Utilization," Hospitals, 32:48–52, October 16, 1953.

Following is an abstract of the article from the Hospital Planning Abstract Service, A.H.A.

Critics of hospitals and of prepayment have argued that much unnecessary hospitalization has occurred because the individual citizen frequently no longer pays his own hospital bill. One method proposed to reduce this problem would be to provide comprehensive prepayment coverage for certain services provided outside the hospital, thus reducing the incentive for hospitalization. It is thought that this would result in a net reduction in costs.

The writer points out that a recent study in New York City appears to confirm this, where the annual hospitalization rate per 1,000 for members of Blue Cross-Blue Shield was found to be 680, while the rate for a comparable group, members of the more comprehensive Blue Cross-Health Insurance Plan combination, was 580. But, argues the writer, the low rate for the group covered by the latter plan is due to the prevailing fee-for-service system of paying physicians. He proposes that data from an area where this system is absent permit him to demonstrate that the rate of hospitalization tends to be higher under comprehensive medical care programs.

In the Canadian province of Saskatchewan the population has had comprehensive hospital insurance with virtually no limitations for more than 10 years. Also, there are a variety of prepaid plans for physicians' services, and information is available on hospitalization rates for these groups as well as for persons without this insurance. Analysis of statistics on comparative groups demonstrates that measured by (1) cases admitted, or (2) days of hospitalization per year, the highest rates exist in the region where prepaid physician care is most complete.

Although the writer concedes that this data from a largely rural province should be used with caution, he is convinced that factors he identifies contribute to increased hospitalization under comprehensive programs also operate in other places. These factors are, he suggests, as follows:

Case finding.—Under prepaid medical care people are more likely to see physicians, and physicians are more likely to discover conditions requiring hospitalization. This would tend to increase the rate of hospitalization.

Timesaving.—The tremendous demands on the time of physicians, increased by prepayment, have tended to force certain timesaving practices on them.

One of these is to hospitalize more of the serious cases and those requiring laboratory work.

DENSON ET AL

Denson, Paul M., Balamuth, Eve, and Shapiro, Sam. "Prepaid Medical Care and Hospital Utilization." Hospital Monograph Series No. 3. American Hospital Association, 1958.

A study was made of the hospitalization experience in 1955 of two groups which have the same hospital insurance coverage, but different medical insurance coverage, in order to determine the influence of a program of comprehensive insurance for medical care upon hospital utilization. The two groups selected for the study were those of the health insurance plan of Greater New York (H.I.P.) and the United Medical Service (Blue Shield). A detailed description of the groups by the authors states:

"H.I.P. is provided with comprehensive coverage against the costs of medical care both in and out of the hospital. the care being provided by doctors associated with medical groups; the other population is insured under the Blue Shield contracts for surgical and maternity care and a little more than a third of this group is covered in addition for other in hospital medical care. The medical care for those insured under the Blue Shield contract is provided in the main on a solo practice basis. Both populations are insured against hospital costs under the same type of group contract with Blue Cross."

Among the findings of this study:

Annual number of 1955 hospital admissions per 1,000 population:	
Blue Cross-H.I.P.	77.4
Blue Cross-Blue Shield	95.8
Annual hospital admissions by sex per 1,000 population:	
Males—Blue Cross-H.I.P.	54.0
Blue Cross-Blue Shield	70.8
Females—Blue Cross-H.I.P.	101.2
Blue Cross-Blue Shield	118.7
Days' duration of hospital stay:	
Blue Cross-H.I.P.	7.6
Blue Cross-Blue Shield	7.2

These data are further analyzed by rates of admission by matched employment groups, by diagnosis, and by surgical and nonsurgical conditions, and by other factors.

Dr. HALDEMAN. We had recently completed a review of the literature regarding hospital utilization, and in view of the discussions that were before this committee when surgeon general testified——

Mr. FOGARTY. I think everyone is interested in trying to bring down the hospital costs, but it is a question of how to bring them down. They have gone up tremendously in the last 10 to 15 years, have they not?

Dr. HALDEMAN. Oh, yes. Very much.

Mr. FOGARTY. Do you have any figures on it? I believe someone gave them the other day, but I have forgotten what they were precisely.

Dr. HALDEMAN. General hospital costs per patient day in the past decade have increased by 111 percent, while the Consumer Price Index rose about 22 percent. In 1946 the average length of stay in general hospitals was somewhat over 9 days, and the average hospital bill per admission was $85. In 1959 the average length of stay was reduced to 7.8 days, while the bill increased to $235 per admission.

NEW HOSPITAL DESIGN

Mr. FOGARTY. You heard what I asked Miss Arnstein about this proposal for hospital construction? I understand that you have been out to see the one that is in operation.

Dr. Haldeman. Yes, sir; I have been.

Mr. Fogarty. The proponents of this proposal have asked to testify. They think that they have something, and all of the statistics they showed me last week led me to believe that they might have something too. But I am no expert in this field, and you are. Do you want to tell us about that, and what you think?

Dr. Haldeman. Yes. I think the people in Rochester are to be congratulated for having entered into this experimental program. It is something we need a lot more of. I was rather impressed with the design as being an improvement of the conventional nursing unit as far as a unit for the critically ill patients in an intensive care unit is concerned. As I am sure they told you, it needs a good deal more experimentation.

Mr. Fogarty. They thought money should be appropriated to do more research.

Dr. Haldeman. I would agree very much with their view.

Mr. Fogarty. They feel further studies should be made.

Dr. Haldeman. I would agree.

Mr. Fogarty. Do you think it has possibilities of cutting down costs?

Dr. Haldeman. I think the progressive patient care concept has possibilities. The intensive care unit they have designed is a very satisfactory arrangement. It has a number of advantages and it gives the patient a certain amount of privacy, while at the same time he has the feeling of security that goes along with being able to see the nurses.

The advantages from the standpoint of the nurses is that it cuts down on the number of steps and permits them to keep the patients under visual observation most of the time. It has one drawback, which is lack of flexibility, but I would hope——

Mr. Fogarty. What do you mean by lack of flexibility?

Dr. Haldeman. The need for flexibility comes about by virtue of the fact that the total number of patients in a progressive patient care hospital requiring intensive care fluctuates a great deal day by day. If there are an average of 30 patients requiring this type of care there will be some days in a month when there will be only 15 patients, and there will be other days when census of the unit will be up to 45. An intensive care unit that is so designed that it can be contracted or expanded will frequently be able to make provisions for the intermediate-care patients should the intermediate-care unit be filled to capacity. I think that it should be quite possible to design a unit which takes advantage of the good points of the circular nursing unit design, and also will build in flexibility. I think that is the reason why the Rochester people need to do additional research and should be encouraged to do it.

Mr. Fogarty. Have you any ideas that are better than this?

Dr. Haldeman. The current Public Health Service guide materials describing progressive patient care separate those patients who are critically ill into two groups—those requiring constant supervision and those who do not. We prefer and recommend that those requiring constant supervision should be located in a room with on an average of six patients. In this same room a nursing station is provided, thereby making it possible to provide constant nursing care to critically ill patients in the same area. It has the disadvantage of lack of privacy. However, at Rochester classification of patients for the intensive care units has been different than in some other hospitals. They routinely send their postoperative care patients to this unit, and many of them are not critically ill for a long period of time. Under the classification we usually follow patients are really critically ill, therefore, the lack of privacy is not so important.

Mr. FOGARTY. This looks to me as though it could be used for the intensive care patients, could it not?

Dr. HALDEMAN. It could be. Yes, sir.

Mr. FOGARTY. They said that the doctors liked it.

Dr. HALDEMAN. I can certainly confirm that from talking to them.

Mr. FOGARTY. And the nurses like it because it cuts down steps. They have some pretty attractive statistics, and this study has been going on for 5 or 6 years, has it not?

Dr. HALDEMAN. Yes.

Mr. FOGARTY. It was started by the people out at Mayo's. They have received some grants from a private foundation.

Dr. HALDEMAN. Yes, sir; from the Kellogg Foundation, I believe.

Mr. FOGARTY. They were thinking that the Federal Government might be interested in assisting in building others for further study. If they come here a month from now and give us all of these statistics, how are we to know if it is good or not? You do not seem to be very enthusiastic about it.

Dr. HALDEMAN. I certainly hope I did not give the impression that I did not feel it was promising.

Mr. FOGARTY. It costs about $10 or $12 million to get one of these going, but if it would cut costs as they say it would, it would be cheap at twice the price.

Dr. HALDEMAN. You know that the administration feels we should encourage not only research, but research and experimental design. For that reason we have as a part of the Community Services Facilities Act a request by the Congress to remove the ceiling from our hospital research funds, and also to authorize nonformula construction grants for research or demonstration facilities. This is the very sort of thing we had in mind. I certainly did not intend to give the impression that this is not a worthwhile avenue of investigation. If I sounded cautious it is due to the fact that I did not want to give people, planning hospitals in the country at large, the impression that this was the solution to hospital design on the basis of present knowledge. Could I go off the record a moment?

Mr. FOGARTY. Yes.

(Discussion off the record.)

NEED FOR GENERAL HOSPITAL FACILITIES

Mr. FOGARTY. Has the need and demand for general hospital facilities gone down?

Dr. HALDEMAN. No, sir, Mr. Chairman.

Mr. FOGARTY. As I understand, the population increase will require about 42,000 additional hospital and nursing home beds every year?

Dr. HALDEMAN. That is right. It is 42,000 for the population increase.

Mr. FOGARTY. And 26,000 beds become obsolete every year?

Dr. HALDEMAN. That is correct.

Mr. **Fogarty.** That would bring it up to 68,000 total?

Dr. **Haldeman.** Yes.

Mr. **Fogarty.** As of June 30, 1960, State plans showed a need for 1,120,000 additional hospital and nursing home beds. In your amended budget the request for part C and nursing homes is $135 million, or $25 million less than appropriated for 1961. Is that right?

Dr. **Haldeman.** That is correct, sir.

Mr. **Fogarty.** You are going backwards instead of ahead, according to my arithmetic.

Dr. **Haldeman.** In terms of general hospital beds?

Mr. **Fogarty.** Yes; and the need.

Dr. **Haldeman.** As I explained earlier, it will, however, permit us to move ahead more rapidly in terms of long-term and ambulatory care facilities.

Mr. **Fogarty.** Your request in total is $185 million and the States say they can match $471 million. Is that correct?

Dr. **Haldeman.** That is correct.

Mr. **Fogarty.** So we are not keeping up with this kind of a budget.

HOSPITAL RESEARCH

The request for research is $1,200,000 but you have legislation that would remove that ceiling.

Dr. **Haldeman.** That is correct.

Mr. **Fogarty.** How much do you think we should be spending on research?

Dr. **Haldeman.** Hospitals are a big business and we spend now about $8 billion a year on providing care in the Nation's hospitals. They employ approximately a million and a half people, which is the equivalent to those employed in the steel industry and the automobile industry combined. We are spending, I believe, over $700 million now a year on medical research, and yet in the field of hospital research we are possibly spending $3 million a year every year. I feel a desirable goal would be to spend one-half of 1 percent of what we are providing for patient care in the field of hospital research, which would mean that the country as a whole should be spending in the neighborhood of $40 million for hospital research. We could not reach that level immediately, but I think it is fairly conservative compared to industry. The pharmaceutical industry, for instance, ploughs back 3 to 5 percent of its income into research in the area.

OPERATIONS AND TECHNICAL SERVICES

Mr. **Fogarty.** The amount for "Operations and technical services" is $1,736,000 for 1961. The request for 1962 is $1,772,000, an increase of $36,000. No new positions are requested, are there?

Dr. **Haldeman.** No, sir. The increase of $36,000 is a small amount for annualization, but the bulk of it, $34,000 of it, is to compensate for the absorption of Pay Act increases.

Mr. **Fogarty.** Is that the explanation you have in the justifications—"Restoration of program reduction resulting from absorption of Pay Act costs in 1961"?

Dr. **Haldeman.** That is correct, sir.

Mr. **Fogarty**. In 1961 you were made to absorb these costs. In 1962 you are not?

Dr. **Haldeman**. That is correct.

Mr. **Fogarty**. That seems to be about as consistent as the application of the criteria for amendments to the 1962 budget.

Dr. **Haldeman**. Actually we absorb $35,000 out of the $90 million, and the restoration is only a part of the cost of the Pay Act.

Mr. **Fogarty**. Did you ask for any more money for "Operations and technical services"?

Dr. **Haldeman**. Yes. We requested $322,000 more than was allowed by the Bureau of the Budget.

Mr. **Fogarty**. Why was it not allowed?

Mr. **Kelly**. I guess we just didn't make the justifications persuasive.

Mr. **Fogarty**. You mean it did not meet the criteria?

Mr. **Kelly**. The request was in both the original budget estimate and the amended budget estimate.

Mr. **Fogarty**. But this would not meet the so-called criteria?

Mr. **Kelly**. If it had been related to the increase in the program requirements it might have, but the justification was on the basis of establishing a minimum staff requirement without regard to the current criteria, and was not approved.

BACKLOG OF CONSTRUCTION NEEDS BY STATE

Mr. **Fogarty**. We will put the usual tables in the record showing the needs and matching potential by State.

(The tables referred to follow:)

Summary of anticipated construction of hospitals and other medical facilities (under title VI of the Public Health Service Act) if there were no limitation on Federal assistance for fiscal years 1962 and 1963

State and program year	Number of projects			Beds or units added, by type of project									Estimated cost (thousands)					
				Part C					Part G				Total program		Part C		Part G	
	Total	Part C	Part G	General hospital	Mental hospital	Chronic hospital	TB hospital	Health center (units)	Diagnostic or treatment (units)	Chronic hospital	Rehabilitation facilities (units)	Nursing homes	Total cost	Federal share	Total cost	Federal share	Total cost	Federal share
Total	1,736	1,161	575	67,869	10,216	2,054	791	106	119	4,323	64	17,252	$2,144,581	$883,641	$1,818,157	$745,042	$326,424	$138,599
1962	1,063	718	345	43,754	5,942	892	335	62	62	2,589	45	10,594	1,328,440	471,074	1,124,235	390,894	204,205	80,180
1963	673	443	230	24,115	4,274	1,162	456	44	57	1,734	19	6,658	816,141	412,567	693,922	354,148	122,219	58,419
Alabama	48	35	13	2,072	400	----	50	8	1	30	1	280	44,654	25,436	39,224	21,816	5,430	3,620
1962	26	18	8	1,177	----	----	----	3	----	30	1	130	24,728	12,552	21,218	10,212	3,510	2,340
1963	22	17	5	895	400	----	50	5	1	----	----	150	19,926	12,884	18,006	11,604	1,920	1,280
Alaska	11	8	3	322	----	----	----	3	1	174	----	----	14,858	6,345	10,008	3,900	4,850	2,445
1962	9	7	2	110	----	----	----	3	1	66	----	----	5,658	2,395	3,508	1,300	2,150	1,095
1963	2	1	1	212	----	----	----	----	----	108	----	----	9,200	3,950	6,500	2,600	2,700	1,350
Arizona	12	8	4	403	----	----	200	2	----	----	1	100	12,226	5,238	10,682	4,466	1,544	772
1962	10	6	4	333	----	----	200	1	----	----	1	100	10,326	4,288	8,782	3,516	1,544	772
1963	2	2	----	70	----	----	----	1	----	----	----	----	1,900	950	1,900	950	----	----
Arkansas	28	23	5	672	500	----	----	1	----	----	5	----	16,026	8,680	15,035	7,792	991	888
1962	14	12	2	337	----	----	----	1	----	----	2	----	5,866	3,498	5,485	3,017	381	481
1963	14	11	3	335	500	----	----	----	----	----	3	----	10,160	5,182	9,550	4,775	610	407
California	119	82	37	5,805	510	----	80	10	8	----	5	1,447	169,377	51,096	138,369	44,006	31,008	7,090
1962	68	48	20	3,196	365	----	80	5	7	----	1	622	95,961	26,614	75,512	23,061	20,449	3,553
1963	51	34	17	2,609	145	----	----	5	1	----	4	825	73,416	24,482	62,857	20,935	10,559	3,537

Colorado	29	23	6	2, 424	673			2				240	76, 139	34, 302	73, 719	33, 090	2, 420	1, 212
1962	29	23	6	2, 424	673			2				240	76, 139	17, 151	73, 719	16, 545	2, 420	606
1963														17, 151		16, 545		606
Connecticut	12	6	6	314					4	30		64	23, 353	5, 982	19, 269	5, 222	4, 084	760
1962	12	6	6	314					4	30		64	23, 353	4, 174	19, 269	3, 497	4, 084	677
1963														1, 808		1, 725		83
Delaware	4	3	1										3, 965	1, 050	2, 365	250	1, 600	800
1962	4	3	1										3, 965	1, 050	2, 365	250	1, 600	800
1963																		
District of Columbia	4	2	2			300		1			2		5, 400	2, 533	5, 270	2, 468	130	65
1962																		
1963	4	2	2			300		1			2		5, 400	2, 533	5, 270	2, 468	130	65
Florida	45	36	9	3, 844				2	4	600		150	78, 421	29, 167	64, 221	21, 792	14, 200	7, 375
1962	41	35	6	3, 644				2	2	400		150	69, 621	16, 647	60, 221	13, 522	9, 400	3, 125
1963	4	1	3	200					2	200			8, 800	12, 520	4, 000	8, 270	4, 800	4, 250
Georgia	38	33	5	1, 454	50					75	2	100	34, 389	15, 140	31, 164	13, 528	3, 225	1, 612
1962	30	25	5	1, 002	50					75	2	100	25, 049	11, 030	21, 824	9, 418	3, 225	1, 612
1963	8	8		452									9, 340	4, 110	9. 340	4, 110		
Hawaii	16	10	6	142	25			3	1	96	1	230	8, 766	5, 302	6, 050	4, 036	2, 716	1, 266
1962	5	3	2	67				1			1	100	2, 186	1, 812	1, 220	1, 421	966	391
1963	11	7	4	75	25			2	1	96		130	6, 580	3, 490	4, 830	2, 615	1, 750	875
Idaho	16	8	8	122					3			405	6, 305	3, 669	2, 355	1, 694	3, 950	1, 975
1962	16	8	8	122					3			405	6, 305	3, 669	2, 355	1, 694	3, 950	1, 975
1963																		
Illinois	45	25	20	1, 505	60			1	4	280	2	350	50, 930	16, 973	39. 590	13, 196	11, 340	3, 777
1962	24	13	11	785	30				2	120	2	160	28, 040	9, 344	22, 530	7, 509	5, 510	1, 835
1963	21	12	9	720	30			1	2	160		190	22, 890	7, 629	17, 060	5, 687	5, 830	1, 942
Indiana	38	20	18	1, 556	44				9	300	1	133	53, 251	16, 989	49, 771	15, 896	3, 480	1, 093
1962	24	13	11	1, 226	30				5	300	1	77	41, 778	13, 222	39, 258	12, 393	2, 520	829
1963	14	7	7	330	14				4			56	11, 473	3, 767	10, 513	3, 503	960	264

Summary of anticipated construction of hospitals and other medical facilities (under title VI of the Public Health Service Act) if there were no limitation on Federal assistance for fiscal years 1962 and 1963—Continued

State and program year	Number of projects			Beds or units added, by type of project									Estimated cost (thousands)					
				Part C					Part G				Total program		Part C		Part G	
	Total	Part C	Part G	General hospital	Mental hospital	Chronic hospital	TB hospital	Health center (units)	Diagnostic or treatment (units)	Chronic hospital	Rehabilitation facilities (units)	Nursing homes	Total cost	Federal share	Total cost	Federal share	Total cost	Federal share
Iowa	33	15	18	580	35	120	-----	-----	-----	-----	-----	780	$25, 125	$8, 375	$15, 525	$5, 175	$9, 600	$3, 200
1962	21	11	10	450	-----	-----	-----	-----	-----	-----	-----	460	15, 195	5, 065	9, 225	3, 075	5, 970	1, 990
1963	12	4	8	130	35	120	-----	-----	-----	-----	-----	320	9, 930	3, 310	6, 300	2, 100	3, 630	1, 210
Kansas	23	14	9	200	-----	75	-----	-----	-----	-----	1	385	28, 600	13, 800	24, 000	11, 500	4, 600	2, 300
1962	10	7	3	-----	-----	-----	-----	-----	-----	-----	1	100	11, 900	5, 450	10, 100	4, 550	1, 800	900
1963	13	7	6	200	-----	75	-----	-----	-----	-----	-----	285	16, 700	8, 350	13, 900	6, 950	2, 800	1, 400
Kentucky	35	32	3	1, 255	300	-----	-----	-----	-----	-----	-----	165	26, 750	13, 916	25, 100	12, 337	1, 650	1, 579
1962	22	21	1	845	200	-----	-----	-----	-----	-----	-----	75	18, 450	8, 939	17, 700	8, 187	750	752
1963	13	11	2	410	100	-----	-----	-----	-----	-----	-----	90	8, 300	4, 977	7, 400	4, 150	900	827
Louisiana	38	26	12	2, 325	1, 100	-----	-----	-----	3	-----	2	200	69, 580	34, 350	63. 380	31, 250	6, 200	3. 100
1962	18	10	8	1, 215	-----	-----	-----	-----	2	-----	1	200	27, 300	13, 650	22, 800	11, 400	4, 500	2, 250
1963	20	16	4	1, 110	1, 000	-----	-----	-----	1	-----	1	-----	42, 280	20, 700	40, 580	19, 850	1, 700	850
Maine	21	16	5	510	-----	-----	81	-----	1	-----	-----	80	14, 300	7, 150	12, 300	6. 150	2, 000	1. 000
1962	10	8	2	262	-----	-----	25	-----	-----	-----	-----	50	6, 300	3, 150	5, 800	2, 900	500	250
1963	11	8	3	248	-----	-----	56	-----	1	-----	-----	30	8, 000	4, 000	6, 500	3. 250	1, 500	750
Maryland	27	19	8	2, 194	1, 200	-----	-----	2	-----	66	3	65	79, 514	25, 418	76, 614	24, 005	2, 900	1, 413
1962	25	18	7	2, 194	1. 200	-----	-----	1	-----	66	3	40	79, 184	13, 052	76, 404	12, 179	2, 780	873
1963	2	1	1	-----	-----	-----	-----	1	-----	-----	-----	25	330	12, 366	210	11, 826	120	540
Massachusetts	52	36	16	1, 477	-----	300	-----	1	15	-----	1	-----	52, 270	20, 908	45, 620	18, 248	6, 650	2, 660
1962	12	12	-----	587	-----	-----	-----	-----	-----	-----	-----	-----	11, 870	4, 446	11, 870	4, 446	-----	-----

1963	40	24	16	890		300		1	15		1		40,400	16,462	33,750	13,802	6,650	2,660
Michigan	78	56	22	4,319	1,335			5	3	415	1	810	122,110	45,571	108,260	38,646	13,850	6,925
1962	30	22	8	1,447	180					200		280	36,307	14,018	32,157	11,943	4,150	2,075
1963	48	34	14	2,872	1,155			5	3	215	1	530	85,803	31,553	76,103	26,703	9,700	4,850
Minnesota	135	39	96	2,595						135	4	4,826	113,847	49,961	71,138	30,739	42,709	19,222
1962	88	27	61	1,016						60	3	3,051	57,966	24,813	31,938	13,098	26,028	11,715
1963	47	12	35	1,579						75	1	1,775	55,881	25,148	39,200	17,641	16,681	7,507
Mississippi	27	27		1,330				8					21,630	14,370	21,630	14,370		
1962	26	26		1,330				8					21,330	12,630	21,330	12,630		
1963	1	1											300	1,740	300	1,740		
Missouri	33	19	14	936	357	154			5		2	550	40,268	26,814	30,257	21,808	10,011	5,006
1962	18	7	11	319	304	79			4		2	450	29,808	17,822	22,591	14,213	7,217	3,609
1963	15	12	3	617	53	75			1			100	10,460	8,992	7,666	7,595	2,794	1,397
Montana	7	5	2	309	30					50		80	8,210	2,884	7,110	2,444	1,100	440
1962	7	5	2	309	30					50		80	8,210	1,442	7,110	1,222	1,100	220
1963														1,442		1,222		220
Nebraska	33	20	13	491		360		3	1			420	19,581	7,832	15,426	6,170	4,155	1,662
1962	18	12	6	399		360		1	1			120	15,426	6,170	13,176	5,270	2,250	900
1963	15	8	7	92				2				300	4,155	1,662	2,250	900	1,905	762
Nevada	8	4	4	210			30					146	8,130	3,603	6,300	2,688	1,830	915
1962	5	2	3	140			30					126	6,130	2,593	4,700	1,878	1,430	715
1963	3	2	1	70								20	2,000	1,010	1,600	810	400	200
New Hampshire	20	11	9	443					5		1	150	10,550	3,380	8,310	2,460	2,240	920
1962	9	4	5	150					2		1	100	4,750	840	3,450	550	1,300	290
1963	11	7	4	293					3			50	5,800	2,540	4,860	1,910	940	630
New Jersey	38	21	17	2,169	220			1	8		4	326	50,120	16,768	40,048	13,245	10,072	3,523
1962	28	16	12	1,819	220				7		4	100	40,219	13,302	33,639	11,001	6,580	2,301
1963	10	5	5	350				1	1			226	9,901	3,466	6,409	2,244	3,492	1,222
New Mexico	19	17	2	1,016						145			17,427	8,120	15,977	7,395	1,450	725
1962	12	10	2	651						145			9,402	4,107	7,952	3,382	1,450	725
1963	7	7		365									8,025	4,013	8,025	4,013		

Summary of anticipated construction of hospitals and other medical facilities (under title VI of the Public Health Service Act) if there were no limitation on Federal assistance for fiscal years 1962 and 1963—Continued

State and program year	Number of projects			Beds or units added, by type of project									Estimated cost (thousands)					
				Part C					Part G				Total program		Part C		Part G	
	Total	Part C	Part G	General hospital	Mental hospital	Chronic hospital	TB hospital	Health center (units)	Diagnostic or treatment (units)	Chronic hospital	Rehabilitation facilities (units)	Nursing homes	Total cost	Federal share	Total cost	Federal share	Total cost	Federal share
New York	47	46	1	2,553	472	425	350	------	------	------	------	70	$161,102	$53,701	$160,320	$53,440	$782	$261
1962	21	20	1	557	90	190	------	------	------	------	------	70	33,993	11,331	33,211	11,070	782	261
1963	26	26	------	1,996	382	235	350	------	------	------	------	------	127,109	42,370	127,109	42,370	------	------
North Carolina	33	25	8	1,985	------	------	------	------	4	50	1	110	48,090	23,401	44,540	21,448	3,550	1,953
1962	14	10	4	1,700	------	------	------	------	------	50	1	110	32,390	10,345	30,590	9,355	1,800	990
1963	19	15	4	285	------	------	------	------	4	------	------	------	15,700	13,056	13,950	12,093	1,750	963
North Dakota	11	7	4	140	------	30	------	------	------	------	2	160	8,325	2,555	6,260	1,616	2,065	939
1962	7	3	4	55	------	------	------	------	------	------	2	160	2,747	1,225	682	286	2,065	939
1963	4	4	------	85	------	30	------	------	------	------	------	------	5,578	1,330	5,578	1,330	------	------
Ohio	87	44	43	2,700	60	------	------	5	13	750	3	1,203	97,558	32,483	69,760	23,254	27,798	9,229
1962	40	20	20	1,750	20	------	------	1	6	350	2	540	56,730	18,910	43,383	14,462	13,347	4,448
1963	47	24	23	950	40	------	------	4	7	400	1	663	40,828	13,573	26,377	8,792	14,451	4,781
Oklahoma	21	16	5	555	50	------	------	6	------	------	1	250	14,700	7,350	12,900	6,450	1,800	900
1962	8	6	2	175	50	------	------	------	------	------	------	150	5,000	2,500	4,300	2,150	700	350
1963	13	10	3	380	------	------	------	6	------	------	1	100	9,700	4,850	8,600	4,300	1,100	550
Oregon	16	9	7	300	443	------	------	------	1	395	1	55	16,695	6,283	12,380	4,125	4,315	2,158
1962	8	5	3	150	443	------	------	------	------	240	1	55	7,085	2,720	4,930	1,642	2,155	1,078
1963	8	4	4	150	------	------	------	------	1	155	------	------	9,610	3,563	7,450	2,483	2,160	1,080

Pennsylvania	58	43	15	1,998	10			1	3	102	2	268	89,669	30,180	75,295	25,389	14,374	4,791
1962	58	43	15	1,998	10			1	3	102	2	268	89,669	30,180	75,295	25,389	14,374	4,791
1963																		
Rhode Island	12	8	4	327					2		2		13,900	5,225	8,275	2,625	5,625	2,600
1962	12	8	4	327					2		2		13,900	2,720	8,275	1,420	5,625	1,300
1963														2,505		1,205		1,300
South Carolina	24	20	4	1,310	200				2		1	25	32,200	15,860	30,700	15,350	1,500	510
1962	11	7	4	650	200				2		1	25	18,500	9,010	17,000	8,500	1,500	510
1963	13	13		660									13,700	6,850	13,700	6,850		
South Dakota	19	10	9	211				1			1	310	7,450	4,585	4,650	2,785	2,800	1,800
1962	9	4	5	60				1				210	3,550	2,635	1,800	1,360	1,750	1,275
1963	10	6	4	151							1	100	3,900	1,950	2,850	1,425	1,050	525
Tennessee	6	4	2	130	190			1	1			35	3,261	2,631	2,770	2,376	491	255
1962	6	4	2	130	190			1	1			35	3,261	2,631	2,770	2,376	491	255
1963																		
Texas	59	50	9	3,090	1,380					30	2	598	77,200	36,455	66,890	31,300	10,310	5,155
1962	39	30	9	2,300	1,380					30	2	598	64,850	21,930	54,540	17,775	10,310	4,155
1963	20	20		790									12,350	14,525	12,350	13,525		1,000
Utah	29	27	2	1,170	200	80						150	47,150	23,388	45,950	22,788	1,200	600
1962	29	27	2	1,170	200	80						150	47,150	21,388	45,950	20,788	1,200	600
1963														2,000		2,000		
Vermont	12	8	4	71	25				2			66	3,732	1,696	2,392	797	1,340	899
1962	5	4	1						1				990	600	740	246	250	354
1963	7	4	3	71	25				1			66	2,742	1,096	1,652	551	1,090	545
Virginia	22	18	4	1,486				7		190		150	37,480	17,044	34,880	16,084	2,600	960
1962	22	18	4	1,486				7		190		150	37,480	9,585	34,880	8,625	2,600	960
1963														7,459		7,459		
Washington	28	25	3	1,262				2			1	85	34,050	13,770	29,410	11,914	4,640	1,856
1962	14	13	1	482				2			1		12,750	5,250	12,310	5,074	440	176
1963	14	12	2	780								85	21,300	8,520	17,100	6,840	4,200	1,680

Summary of anticipated construction of hospitals and other medical facilities (under title VI of the Public Health Service Act) if there were no limitation on Federal assistance for fiscal years 1962 and 1963—Continued

State and program year	Number of projects			Beds or units added, by type of project									Estimated cost (thousands)					
				Part C					Part G				Total program		Part C		Part G	
	Total	Part C	Part G	General hospital	Mental hospital	Chronic hospital	TB hospital	Health center (units)	Diagnosic or treatment (units)	Chronic hospital	Rehabilitation facilities (units)	Nursing homes	Total cost	Federal share	Total cost	Federal share	Total cost	Federal share
West Virginia	30	22	8	787	47	210	------	4	6	------	2	------	$24, 999	$12, 274	$21, 743	$10, 646	$3, 256	$1, 628
1962	13	9	4	319	27	183	------	1	2	------	2	------	13, 549	6, 549	11, 343	5, 446	2, 206	1, 103
1963	17	13	4	468	20	27	------	3	4	------	------	------	11, 450	5, 725	10, 400	5, 200	1, 050	525
Wisconsin	71	33	38	2, 086	50	------	------	------	6	210	4	979	77, 725	31, 090	57, 375	22, 950	20, 350	8, 140
1962	39	19	20	1, 276	50	------	------	------	4	85	2	462	47, 150	17, 860	36, 425	13, 570	10, 725	4, 290
1963	32	14	18	810	------	------	------	------	2	125	2	517	30, 575	13, 230	20, 950	9, 380	9, 625	3, 850
Wyoming	6	4	2	75	------	------	------	------	------	------	------	56	2, 280	560	1, 750	320	530	240
1962	5	4	1	75	------	------	------	------	------	------	------	31	2, 120	410	1, 750	250	370	160
1963	1	------	1	------	------	------	------	------	------	------	------	25	160	150	------	70	160	80
Guam	6	6	------	------	------	------	------	6	------	------	------	------	210	140	210	140	------	------
1962	3	3	------	------	------	------	------	3	------	------	------	------	105	70	105	70	------	------
1963	3	3	------	------	------	------	------	3	------	------	------	------	105	70	105	70	------	------
Puerto Rico	47	37	10	2, 639	250	------	------	20	3	200	2	200	40, 733	31, 848	35, 620	27, 463	5, 113	4, 385
1962	29	23	6	1, 224	------	------	------	17	1	------	1	200	16, 749	14, 290	14, 748	11, 761	2, 001	2, 529
1963	18	14	4	1, 415	250	------	------	3	2	200	1	------	23, 984	17, 558	20, 872	15, 702	3, 112	1, 856
Virgin Islands	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------
1962 [1]	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------
1963 [1]	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------

[1] No information.

Source: State agency reports to the Public Health Service.

Civilian hospital and nursing home beds [1] in the United States and possessions, 1948–61

Category and year [2]	Total beds needed [3]	Existing beds				Additional beds needed
		Total	Acceptable		Nonacceptable [4]	
			Number	Percent of total need		
ALL CATEGORIES (INCLUDING NURSING HOMES)						
1961	2,501,406	1,703,825	1,376,048	55.0	327,777	1,108,920
1960	2,464,800	1,641,191	1,346,059	54.6	295,132	1,102,432
1959	2,412,802	1,568,028	1,286,489	53.3	281,539	1,119,165
1958	2,444,726	1,521,267	1,238,188	50.6	283,079	1,211.141
1957	2,399,060	1,505,034	1,219,885	50.8	285,149	1,184,245
HOSPITAL CATEGORIES						
1961	2,054,458	1,378,035	1,194,983	58.2	183,052	843,037
1960	2,037,629	1,350,212	1,175,918	57.7	174,294	845,402
1959	2,027,750	1,322,197	1,153,473	56.9	168,724	867,129
1958	2,009,040	1,299,832	1,125,169	56.0	174,663	888,474
1957	1,985,354	1,287,051	1,106,991	55.8	180,060	883,433
1956	1,960,410	1,279,050	1,117,933	57.0	161,117	850,061
1955	1,926,600	1,275,072	1,098,815	57.0	176,257	838,745
1954	1,887,372	1,242,087	1,083,056	57.4	159,031	812,765
1952	1,899,806	1,193,836	1,017,823	53.6	176,013	881,983
1950	1,850,052	1,118,535	952,196	51.5	166,339	897,856
1948	1,776,401	1,016,712	867,960	48.9	148,752	908,441
GENERAL HOSPITALS						
1961	778,081	694,696	619,666	79.6	75,030	158,415
1960	765,765	678,481	607,338	79.3	71,143	158,427
1959	761,610	653,082	587,318	77.1	65,764	174,292
1958	745,016	632,674	559,818	75.1	72,856	185,776
1957	726,821	620,922	547,473	75.3	73,449	179,926
1956	722,112	614,020	541,363	75.0	72,657	180,749
1955	720,001	601,241	526,458	73.1	74,783	193,543
1954	704,400	589,565	515,934	73.2	73,631	188,420
1952	708,574	554.084	474,334	66.9	79,750	234,240
1950	682,601	513,814	437,786	64.1	76,028	244,815
1948	652,974	469,398	388,144	59.4	81,254	264,830
MENTAL HOSPITALS						
1961	884,721	554,775	456,940	51.6	97,835	427,781
1960	870,313	541.931	449,532	51.7	92,399	420,781
1959	855,649	533,587	445,009	52.0	88,578	412,574
1958	840,782	528.406	441,691	52.5	86,715	400,719
1957	821,412	525,455	435,453	53.0	90,002	387,587
1956	808,265	520,010	449.706	55.6	70,304	359,223
1955	793,125	513,278	441,440	55.7	71,838	352,349
1954	773,428	500,568	437,659	56.6	62.909	336,989
1952	755,097	482,733	412,932	54.7	69,801	342,165
1950	725,203	462,859	399,138	55.0	63,721	326,065
1948	690,381	427,201	380,343	55.1	46,858	310,038
TUBERCULOSIS HOSPITALS						
1961	94,504	72,893	68,768	72.8	4,125	9,298
1960	101,347	78,334	73,274	72.3	5,060	11,764
1959	104.555	84,445	76.685	73.3	7,760	18,788
1958	114.449	87,967	79,523	69.5	8,444	37,323
1957	119,653	91,301	81,491	68.1	9,810	41,026
1956	114,536	96,268	84,923	74.1	11,345	36,533
1955	96,507	100,234	85,901	89.0	14,333	20,902
1954	100,467	101,425	86,035	85.6	15,390	21,707
1952	133,899	99,147	87,550	65.4	11,597	46,349
1950	148,936	94,024	81,511	54.7	12.513	67,425
1948	155,987	84,158	71,151	45.6	13,007	84,836
CHRONIC HOSPITALS						
1961	297,152	55,671	49,609	16.7	6,062	247,543
1960	300,204	51,466	45,774	15.2	5,692	254,430
1959	305,936	51,083	44,461	14.5	6,622	261,475
1958	308,793	50,785	44,137	14.3	6,648	264,656
1957	317,468	49,373	42,574	13.7	6,799	274,894
1956	315,497	48,752	41,941	13.3	6,811	273,556
1955	316,967	60,319	45,016	14.2	15,303	271,951
1954	309,077	50,529	43,428	14.1	7,101	265,649
1952	302,236	57,872	43,007	14.2	14,865	259,229
1950	293,312	47,838	33,761	11.5	14,077	259,551
1948	277,059	35,955	28,322	10.2	7,633	248,737

See footnotes at end of table, p. 216.

Civilian hospital and nursing home beds[1] *in the United States and possessions, 1948–61*—Continued

Category and year [2]	Total beds needed [3]	Existing beds				Additional beds needed
		Total	Acceptable		Nonacceptable [4]	
			Number	Percent of total need		
NURSING HOMES CATEGORY						
1961	446,948	325,790	181,065	40.5	144,725	265,883
1960	427,171	290,979	170,141	39.8	120,838	257,030
1959	385,052	245,831	133,016	34.5	112,815	252,036
1958	435,686	221,435	113,019	25.9	108,416	322,667
1957	413,706	217,983	112,894	27.3	105,089	300,812

[1] Excluding Federal facilities.

[2] As of Jan. 1, each year.

[3] Set by title VI of the Public Health Service Act and regulations thereunder. For some categories, certain States now have beds in excess of current standards of need.

[4] Classified by State agencies, on the basis of fire and health hazards.

Source: State plans for hospital construction, approved under title VI of the Public Health Service Act.

Mr. Fogarty. Mr. Denton.

FACILITIES OTHER THAN GENERAL HOSPITALS

Mr. Denton. For some time you had difficulty in getting communities to build diagnostic centers, rehabilitation centers, and nursing homes. How is that program coming now? Do you have a waiting list on that?

Dr. Haldeman. Oh, yes. The demand is still not uniformly high, but many, many States have a large waiting list, particularly for nursing homes and chronic disease hospitals. Generally speaking, there is a very large demand for long-term care facilities as well as ambulatory care facilities. The demand for rehabilitation facilities is somewhat less. Not that the need does not exist, but there is a greater difficulty in getting sufficient funds for maintenance and operation of these facilities.

Mr. Denton. Do you have much of a waiting list on diagnostic centers and rehabilitation centers?

Dr. Haldeman. Yes. As you know, the bulk of our diagnostic and treatment centers is actually outpatient departments of general hospitals. Between 1953 and 1958 the number of visits to outpatient departments of hospitals increased by almost 50 percent. The number of visits to emergency departments over this period increased by 100 percent. There is a marked upsurge in the utilization of hospital outpatient departments by private physicians for their private patients. The purpose of a hospital is to bring scientific medicine and the private physician together, and with the increasing complexity of the diagnostic procedures required for modern medicine, hospital outpatient departments are being utilized more all the time.

Mr. Denton. Then the diagnostic centers and convalescent centers are really part of hospitals?

Dr. Haldeman. I look upon the whole complex of hospital facilities as something that has to be planned for together. You cannot plan for one without the other, because the demand for one affects the demand and the utilization of the other, so I do not think that you can separate facilities into different categories for the purpose of broad areawide planning.

Mr. DENTON. Do you put nursing homes in the same category?

Dr. HALDEMAN. I certainly would.

FEDERAL DESIGN REQUIREMENTS

Mr. DENTON. In my hometown your department made a grant to a lady building a nursing home for $75,000. She said she had so much trouble with the plans that she just found it better to go ahead and build it without the grant from the Government. She has a very nice nursing home, I should say. What would you say about that?

Dr. HALDEMAN. Our minimum requirements are such that if anyone is going to build a skilled nursing home I could not imagine why they would want to go ahead without a grant.

Mr. DENTON. It is difficult. She said they went over the plans three times. The location of the kitchen was one thing and then there was something else. She had a very good architect doing it too. It is in Evansville, Ind., the Bethlehem Sanitarium.

Dr. HALDEMAN. I am not familiar with the individual case.

Mr. DENTON. And they are building another one there without any trouble. That is all.

Mr. MICHEL. To follow up Mr. Denton's question, Doctor: At Peoria we have the Forest Park Foundation, which did a considerable amount of work in the design of housing for the elderly, and also in rehabilitation work. They likewise have come to me and told me, that some of the restrictions that are imposed upon them are just completely unrealistic. The size of the doors is an example. They made all kinds of regulations which the foundation found from their own research and studies are not necessary at all. They feel that so many times we are putting the builder, and everybody else who wants to do something in this field, in a straitjacket, with no flexibility.

Dr. HALDEMAN. Perhaps it would help some, Mr. Michel, to discuss the background of the development of our minimum standards of construction equipment. I might say earlier in the program, in 1946, we were criticized on occasion for having requirements that were too high. Frankly, we are more frequently criticized now for having requirements that are too low. But these standards of construction equipment were developed after taking the full professional judgment of an advisory committee of experts in the field. These standards were then approved by the Federal Hospital Council.

Most people who are unhappy with the minimum requirements in the nursing home field are sponsors who wish to build a facility which is not primarily aimed at providing skilled nursing services under medical supervision. In other words, our Hill-Burton nursing homes as contrasted to convalescent homes are aimed at people requiring a fair degree of rehabilitation. An applicant who wishes to build what we would call a convalescent home would be unhappy, because we require space which would permit rehabilitation activities. There is the need for the other type of facility, but our funds have been so limited we feel we must confine them to facilities which have an active program of rehabilitation.

Mr. MICHEL. I gather in hearing your testimony that one could well take a rather optimistic view of what progress is being made in hospital construction around the country. Although the chairman would differ with you and think we are not doing enough, I am flexible of mind, and I would like to be convinced one way or another. But I do get some measure of optimism from the tenor of your remarks. Is that correct?

Dr. HALDEMAN. In the general hospital field we have made a good deal of progress about overcoming the shortage of beds, particularly in rural areas; although there are still areas that are very short of beds. However, in the general hospital category in our metropolitan areas obsolescence is a tremendous problem, and one for which a lot needs to be done. But in the area of general hospital beds in rural areas, we have made a lot of progress.

Mr. MICHEL. That is all.

Mr. FOGARTY. You made progress in the rural areas, but the overall bed shortage is going up. You used to tell us you had a shortage of 800,000 or 900,000 beds, and now it is up to 1,100,000. Also, I thought the law should be amended so that some of the existing hospitals could be renovated so that metropolitan hospitals may get some help along that line. What is the administration's stand on that?

Dr. HALDEMAN. The administration has introduced the community facilities services bill, and they have been so busy working on that and other legislation that we have not had an opportunity to work with them in the development of a broad legislative package in the Hill-Burton area.

Mr. FOGARTY. When does the Hill-Burton law expire?

Dr. HALDEMAN. 1964. We have been developing background data. We did a nationwide survey on needs for modernization and on the replacement of obsolete facilities, without adding any beds, and the total amount of money that the survey showed would be needed was $3,600 million.

Mr. FOGARTY. Three billion?

Dr. HALDEMAN. Yes. We included every community having over 2,000 beds in the 25 largest towns, and a sample of other towns. We found that the need in the modernization area is considerable. I am confident that the Department will give every consideration to the need for a legislative program which would be of assistance in this area.

Mr. FOGARTY. You could use $211 million if you had it, could you not?

Dr. HALDEMAN. Yes, sir.

Mr. FOGARTY. Without any trouble? Plans have already been approved?

Dr. HALDEMAN. We have projects——

Mr. FOGARTY. And you asked for that.

Is there anything else you would like to say?

Dr. HALDEMAN. No, sir.

Mr. FOGARTY. Thank you very much.

AMENDMENT TO THE 1962 BUDGET

Note: Following is the formal justification for the amendment to the 1962 budget:

Budget page	Heading	Original estimate	Revised estimate	Increase
643	Hospital construction activities, limitations on: Grants	$152,972,000	$187,972,000	$35,000,000
	(a) Construction, part C	(115,000,000)	(125,000,000)	(10,000,000)
	(b) Construction, part G	(35,000,000)	(60,000,000)	(25,000,000)
	(1) Chronic disease hospitals	(12,500,000)	(20,000,000)	(7,500,000)
	(2) Diagnostic or treatment centers	(7,500,000)	(20,000,000)	(12,500,000)
	(3) Rehabilitation facilities	(5,000,000)	(10,000,000)	(5,000,000)

Program and financing

[In thousands]

	Original 1962 estimate	Revised 1962 estimate	Increase
Program by activities: Operating costs:			
1. Grants:			
(a) Construction, part C	$134,500	$137,500	$3,000
(b) Construction, part G:			
(1) Chronic disease hospitals	9,000	11,250	2,250
(2) Diagnostic or treatment centers	7,500	11,250	3,750
(3) Rehabilitation facilities	8,500	10,000	1,500
(4) Nursing homes	10,000	10,000	
Total construction grants	169,500	180,000	10,500
2. Hospital and medical facilities research	1,200	1,200	
3. Operations and technical services	1,772	1,772	
Total obligations	172,472	182,972	10,500
Financing:			
Unobligated balance brought forward	−124,500	−124,500	
Unobligated balance carried forward	105,000	129,500	24,500
New obligational authority (appropriation)	152,972	187,972	35,000

Object classification

[In thousands]

		Original 1962 estimate	Revised 1962 estimate	Increase
11	Personnel compensation:			
	Permanent positions	$1,559	$1,559	
	Positions other than permanent	27	27	
	Total personnel compensation	1,586	1,586	
12	Personnel benefits	100	100	
21	Travel and transportation of persons	135	135	
22	Transportation of things	6	6	
23	Rent, communications, and utilities	14	14	
24	Printing and reproduction	19	19	
25	Other services	32	32	
	Payment to "Bureau of State Services management fund"	59	59	
26	Supplies and materials	11	11	
31	Equipment	10	10	
33	Investments and loans	500	500	
41	Grants, subsidies, and contributions	170,000	180,500	10,500
	Total obligations	172,472	182,972	10,500

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	194	196	196
Full-time equivalent of other positions	4	4	4
Average number of all employees	178	180	185
Number of employees at end of year	181	191	200
Average GS grade	8.8	9.2	9.2
Average GS salary	$7,280	$8,069	$8,069

GENERAL STATEMENT

An additional request for $35 million to support activities authorized under the hospital and medical facilities survey and construction program is submitted for fiscal year 1962. This request will raise the total estimate for 1962 to $187,972,000 which will provide $125 million for grants or loans to aid in the construction of hospitals, public health centers, and related facilities under part C, $60 million for grants or loans to aid in the construction of medical facilities under part G, $1,200,000 for the hospital and medical facilities research program, and $1,772,000 for operations and technical services. A comparison of the original and revised budgets is shown below:

	Original budget	Revised budget	Increase
Construction grants:			
Hospital and public health centers	$115,000,000	$125,000,000	$10,000,000
Chronic disease hospitals	12,500,000	20,000,000	7,500,000
Nursing homes	10,000,000	10,000,000	0
Diagnostic or treatment centers	7,500,000	20,000,000	12,500,000
Rehabilitation facilities	5,000,000	10,000,000	5,000,000
Hospital and medical facilities research	1,200,000	1,200,000	0
Operations and technical services	1,772,000	1,772,000	0
Total	152,972,000	187,972,000	35,000,000

Hospital and medical facilities construction program—total requested: $185 million

The need and demand for hospitals, nursing homes, diagnostic or treatment centers, and rehabilitation facilities continues at a high level. State agencies reported in January of 1961 that if unlimited Federal funds were available 1,063 projects costing a total of $1.3 billion and utilizing Federal funds in the amount of $471 million could be approved in 1962. The reported need is far in excess of facilities which could be constructed with funds appropriated under the Hill-Burton program. For this reason, and within the limitation of existing appropriation ceilings, the additional amount of $35 million in construction grant funds is distributed among the various categories in such a way as to begin the correction of certain imbalances existing among the various kinds of facilities.

Hospital and public health centers—total requested: $125 million—an increase of $10 million over the original budget request

In 1948 only 59 percent of the general hospital beds needed were in existence whereas in 1960, 79.3 percent of the general beds needed were available. The amount of the requested increase, which will be devoted to general bed construction, will produce an additional 1,335 beds. These additional beds are needed to more nearly maintain the average annual reduction in the deficit of general hospital beds which has occurred since 1948.

The additional funds requested will also permit the construction of some additional mental hospital beds and public health centers. However, the great community pressures for acute general beds force most of these funds into general hospital construction.

Chronic disease hospitals—total requested: $20 million—an increase of $10 million from the original budget request

The need for long-term care beds continues to grow with the increase in our aging population. State agencies report that, as of July 1, 1960, the need exists for 513,389 additional long-term care beds. Additionally, the medical care for the aged program will have a decided impact on the demand for long-term care beds. For this reason, the maximum amount authorized to be appropriated under existing legislation is included in the revised budget. The $10 million increase will construct approximately 1,590 chronic disease beds.

Nursing Homes—total requested, $10 million

This amount is the total authorized to be appropriated under existing legislation. Therefore, no increase is proposed.

Diagnostic or treatment centers—total requested, $20 million—an increase of $12,500,000

The maximum amount authorized to be appropriated for diagnostic or treatment centers is included in the revised budget. This category of facility provides outpatient care for ambulatory facilities and is usually constructed as an outpatient department of a hospital. Greater emphasis in providing outpatient facilities and clinics wil help relieve the pressures for additional and expensive hospital beds. The additional funds requested in the revised budget will permit the construction of an additional 110 centers.

Rehabilitation facilities—total requested, $10 million—an increase of $5 million

The maximum amount authorized to be appropriated is also requested for this category in the revised budget. Rehabilitation facilities provide care on an outpatient basis and also tend to relieve the pressures for additional hospital and long-term care beds. State agencies report that as of July 1, 1960, an additional 200 comprehensive rehabilitation facilities are needed. Data are not avaialble as to the need for the noncomprehensive type of rehabilitation facilities. However, physical medicine departments of hospitals, which include medical, psychological, social, and vocational evaluation services, qualify as rehabilitation facilities, and are sorely needed in many of our hospitals, particuuarly those in urban areas.

The additional funds requested will permit the construction of an additional 25 rehabilitation facilities.

Comparison of projects and beds under the revised and original budgets

The following table compares the projects and beds which could be constructed under the revised and orginal budgets. These computations assume that State agencies will follow the same pattern of project programing as occurred in 1957 and 1958.

Type of project	$185,000,000		$150,000,000		Increase	
	Number of projects	Beds added	Number of projects	Beds added	Number of projects	Beds added
Part C:						
Hospitals	320	18,053	293	16, 606	27	1, 447
Public health centers and laboratories	69	----------	64	----------	5	----------
Total, part C	389	18,053	357	16. 606	32	1, 447
Part G:						
Chronic disease hospitals	87	4, 240	54	2, 650	33	1, 590
Nursing homes	60	2, 920	60	2, 920	----------	----------
Diagnostic or treatment centers	176	----------	66	----------	110	----------
Rehabilitation facilities	49	----------	24	----------	25	----------
Total, part G	372	7, 160	204	5, 570	168	1, 590
Grand total, parts C and G	761	25, 213	561	22, 176	200	3, 037

Hospital and medical facilities research—Total requested $1,200,000

The maximum amount authorized under existing legislation was included in the original budget for hospital research and demonstration activities. No increase is included in the revised budget.

Operations and technical services—Total requested: $1,772,000

No increase is being requested in the revised budget for operations and technical services.

Allocations to States for construction of hospital and medical facilities for fiscal year ending June 30, 1961

State	Total allocation	Allocation under pt. C: Hospitals	Allocation under pt. G: Medical facilities				
			Total allocation under pt. G	Chronic disease hospitals	Diagnostic or treatment centers	Rehabilitation facilities	Nursing homes
Total	$185,000,000	$150,000,000	$35,000,000	$7,500,000	$7,500,000	$10,000,000	$10,000,000
Alabama	5,678,018	4,693,670	984,348	187,080	187,080	305,094	305,094
Alaska	500,000	200,000	300,000	100,000	100,000	50,000	50,000
Arizona	1,698,405	1,326.019	372,386	100,000	100,000	86,193	86,193
Arkansas	3,431,214	2,836,374	594,840	113,052	113,052	184,368	184,368
California	8,329,658	6,885,618	1,444,040	274,446	274,446	447,574	447,574
Colorado	1,863,691	1,472,289	391,402	100,000	100,000	95,701	95,701
Connecticut	1,196,792	882,114	314,678	100,000	100,000	57,339	57,339
Delaware	500,000	200,000	300,000	100,000	100,000	50,000	50,000
District of Columbia	636,600	336,600	300,000	100,000	100,000	50,000	50,000
Florida	5,660,251	4,678,983	981,268	186,494	186,494	304,140	304,140
Georgia	6,150,476	5,084,222	1,066,254	202,646	202,646	330,481	330,481
Hawaii	789,164	489,164	300,000	100,000	100,000	50,000	50,000
Idaho	1,037,943	737,943	300,000	100,000	100,000	50,000	50,000
Illinois	5,953,951	4,921,767	1,032,184	196,171	196,171	319,921	319,921
Indiana	4,365,250	3,608,486	756,764	143,826	143,826	234,556	234,556
Iowa	3,414,534	2,822,586	591,948	112,502	112,502	183,472	183,472
Kansas	2,610,013	2,132,751	477,262	100,000	100,000	138,631	138,631
Kentucky	5,019,005	4,148,905	870,100	165,366	165,366	269,684	269,684
Louisiana	4,832,453	3,994,693	837,760	159,220	159,220	259,660	259,660
Maine	1,365,464	1,031,382	334,082	100,000	100,000	67,041	67,041
Maryland	2,602,393	2,126,007	476,386	100,000	100,000	138,193	138,193
Massachusetts	3,630,819	3,001,377	629,442	119,628	119,628	195,093	195,093
Michigan	5,996,737	4,957,135	1,039,602	197,581	197,581	322,220	322,220
Minnesota	3,840,761	3,174,923	665,838	126,545	126,545	206,374	206,374
Mississippi	4,646,987	3,841,379	805,608	153,109	153,109	249,695	249,695
Missouri	4,385,196	3,624,972	760,224	144,484	144,484	235,628	235,628
Montana	872,790	572,790	300,000	100,000	100,000	50,000	50,000
Nebraska	1,839,642	1,451,008	388,634	100,000	100,000	94,317	94,317
Nevada	500,000	200,000	300,000	100,000	100,000	50,000	50,000
New Hampshire	855,256	555,256	300,000	100,000	100,000	50,000	50.000
New Jersey	3,387,520	2,800,256	587,264	111,612	111,612	182,020	182,020
New Mexico	1,410,850	1,071,546	339,304	100,000	100,000	69,652	69,652
New York	8,846,895	7,313,187	1,533,708	291,488	291,488	475,366	475,366
North Carolina	7,630,942	6,308,032	1,322,910	251,425	251,425	410,030	410.030
North Dakota	1,117,705	812,127	305,578	100,000	100,000	52,789	52,789
Ohio	7,253,302	5,995,860	1,257,442	238,982	238,982	389,739	389,739
Oklahoma	3,133,523	2,590,293	543,230	103,243	103,243	168,372	168,372
Oregon	1,849,296	1,459,550	389,746	100,000	100,000	94,873	94,873
Pennsylvania	10,042,181	8,301,257	1,740,924	330,870	330,870	539,592	539,592

Rhode Island	943, 077	643, 077	300, 000	100, 000	100, 000	50, 000	50, 000
South Carolina	4, 455, 358	3, 682, 970	772, 388	146, 796	146, 796	239, 398	239, 398
South Dakota	1, 217, 282	900, 248	317, 034	100, 000	100, 000	58, 517	58, 517
Tennessee	5, 835, 022	4, 823, 454	1, 011, 568	192, 253	192, 253	313, 531	313, 531
Texas	11, 374, 349	9, 402, 477	1, 971, 872	374, 763	374, 763	611, 173	611, 173
Utah	1, 279, 265	955, 099	324, 166	100, 000	100, 000	62, 083	62, 083
Vermont	720, 376	420, 376	300, 000	100, 000	100, 000	50, 000	50, 000
Virginia	5, 085, 181	4, 203, 607	881, 574	167, 547	167, 547	273, 240	273, 240
Washington	2, 459, 461	1, 999, 519	459, 942	100, 000	100, 000	129, 971	129, 971
West Virginia	2, 817, 467	2, 316, 337	501, 130	100, 000	100, 000	150, 565	150, 565
Wisconsin	4, 111, 437	3, 398, 673	712, 764	135, 464	135, 464	220, 918	220, 918
Wyoming	563, 016	263, 016	300, 000	100, 000	100, 000	50, 000	50, 000
Guam	143, 586	118, 694	24, 892	4, 731	4, 731	7, 715	7, 715
Puerto Rico	5, 050, 916	4, 175, 282	875, 634	166, 418	166, 418	271, 399	271, 399
Virgin Islands	68, 530	56, 650	11, 880	2, 258	2, 258	3, 682	3, 682

Basis of allocations, per statutory formula:

(*a*) Population according to Bureau of the Census 1960 Census of Population Preliminary Reports: Population Counts PC (P1)-1 for States (U.S. summary), and PC (P1)-53, 54, 55, respectively, for Puerto Rico, Guam, and Virgin Islands, August 1960.

(*b*) Allocation percentages for the fiscal years 1960 and 1961, as promulgated in the Federal Register, Sept. 19, 1958.

Tentative allocations to States for construction of hospital and medical facilities for fiscal year ending June 30, 1962

State	Total allocation	Allocation under Pt. C: Hospitals	Allocation under Pt. G: Medical facilities				
			Total allocation under Pt. G	Chronic disease hospitals	Diagnostic or treatment centers	Rehabilitation facilities	Nursing homes
Total	$150,000,000	$115,000,000	$35,000,000	$12,500,000	$7,500,000	$5,000,000	$10,000,000
Alabama	4,568,918	3,581,251	987,667	360,907	185,286	137,393	304,081
Alaska	500,000	200,000	300,000	100,000	100,000	50,000	50,000
Arizona	1,251,667	923,273	328,394	100,000	100,000	50,000	78,394
Arkansas	2,748,873	2,154,647	594,226	217,138	111,477	82,662	182,949
California	7,453,304	5,842,117	1,611,187	588,750	302,258	224,130	496,049
Colorado	1,467,489	1,111,162	356,327	111,979	100,000	50,000	94,348
Connecticut	996,054	687,665	308,389	100,000	100,000	50,000	58,389
Delaware	500,000	200,000	300,000	100,000	100,000	50,000	50,000
District of Columbia	503,489	203,489	300,000	100,000	100,000	50,000	50,000
Florida	4,482,577	3,513,575	969,002	354,087	181,784	134,797	298,334
Georgia	5,042,771	3,952,671	1,090,100	398,338	204,502	151,642	335,618
Hawaii	705,717	405,717	300,000	100,000	100,000	50,000	50,000
Idaho	855,753	555,753	300,000	100,000	100,000	50,000	50,000
Illinois	4,729,748	3,707,314	1,022,434	373,611	191,809	142,229	314,785
Indiana	3,712,677	2,910,104	802,573	293,271	150,563	111,645	247,094
Iowa	2,499,070	1,958,843	540,227	197,406	101,347	75,150	166,324
Kansas	1,957,578	1,517,567	440,011	152,935	100,000	58,221	128,855
Kentucky	3,931,165	3,081,361	849,804	310,530	159,423	118,215	261,636
Louisiana	3,946,675	3,093,519	853,156	311,755	160,052	118,681	262,668
Maine	1,131,577	812,581	318,996	100,000	100,000	50,000	68,996
Maryland	2,022,446	1,570,561	451,885	158,276	100,000	60,254	133,355
Massachusetts	2,999,703	2,351,254	648,449	236,952	121,649	90,205	199,643
Michigan	5,293,454	4,149,163	1,144,291	418,139	214,669	159,181	352,302
Minnesota	3,061,021	2,399,316	661,705	241,796	124,136	92,049	203,724
Mississippi	3,691,750	2,893,701	798,049	291,618	149,714	111,015	245,702
Missouri	3,500,774	2,744,009	756,765	276,532	141,969	105,273	232,991
Montana	753,664	453,664	300,000	100,000	100,000	50,000	50,000
Nebraska	1,302,441	970,073	332,368	100,000	100,000	50,000	82,368
Nevada	500,000	200,000	300,000	100,000	100,000	50,000	50,000
New Hampshire	728,429	428,429	300,000	100,000	100,000	50,000	50,000
New Jersey	2,860,825	2,242,397	618,428	225,982	116,017	86,029	190,400
New Mexico	1,090,509	774,728	315,781	100,000	100,000	50,000	65,781
New York	7,170,572	5,620,504	1,550,068	566,416	290,792	215,628	477,232
North Carolina	6,149,990	4,820,540	1,329,450	485,799	249,405	184,938	409,308
North Dakota	900,231	599,341	300,890	100,000	100,000	50,000	50,890
Ohio	6,142,086	4,814,346	1,327,740	485,174	249,084	184,700	408,782
Oklahoma	2,485,897	1,948,519	537,378	196,365	100,812	74,754	165,447
Oregon	1,468,712	1,112,194	356,518	112,083	100,000	50,000	94,435

Pennsylvania	7, 998, 132	6, 269, 169	1, 728, 963	631, 786	324, 353	240, 514	532, 310
Rhode Island	826, 388	526, 388	300, 000	100, 000	100, 000	50, 000	50, 000
South Carolina	3, 556, 823	2, 787, 941	768, 882	280, 960	144, 243	106, 958	236, 721
South Dakota	945, 405	640, 980	304, 425	100, 000	100, 000	50, 000	54, 425
Tennessee	4, 646, 918	3, 642, 390	1, 004, 528	367, 068	188, 449	139, 739	309, 272
Texas	9, 098, 032	7, 131, 303	1, 966, 729	718, 669	368, 958	273, 589	605, 513
Utah	1, 013, 601	703, 839	309, 762	100, 000	100, 000	50, 000	59, 762
Vermont	629, 896	329, 896	300, 000	100, 000	100, 000	50, 000	50, 000
Virginia	4, 096, 236	3, 210, 749	885, 487	323, 569	166, 117	123, 179	272, 622
Washington	1, 991, 837	1, 545, 555	446, 282	155, 756	100, 000	59, 294	131, 232
West Virginia	2, 162, 431	1, 684, 924	477, 507	169, 801	100, 000	64, 641	143, 065
Wisconsin	3, 213, 653	2, 518, 955	694, 698	253, 852	130, 325	96, 639	213, 882
Wyoming	501, 195	201, 195	300, 000	100, 000	100, 000	50, 000	50, 000
Guam	115, 318	90, 389	24, 929	9, 109	4, 677	3, 463	7, 675
Puerto Rico	4, 041, 359	3, 167, 735	873, 624	319, 234	163, 892	121, 529	268, 969
Virgin Islands	55, 170	43, 244	11, 926	4, 357	2, 238	1, 659	3, 672

NOTE.—Basis of allocations, per statutory formula:

(*a*) Total population according to Bureau of the Census 1960 Census of Population Advance reports: Final Population Counts PC (A1)-1 for States (U.S. summary, dated Nov. 15, 1960). Guam, Puerto Rico, and Virgin Islands based on 1960 census as certified to the Public Health Service by the Bureau of the Census.

(*b*) Allocation percentages for the fiscal years 1962 and 1963, as promulgated in the Federal Register, Sept. 10, 1960.

Tentative allocations to States for construction of hospital and medical facilities for fiscal year ending June 30, 1962—Continued

State	Total allocation	Allocation under Pt. C: Hospitals	Allocation under Pt. G: Medical facilities				
			Total allocation under Pt. G	Diagnostic or treatment centers	Chronic disease hospitals	Rehabilitation facilities	Nursing homes
Total	$185,000,000	$125,000,000	$60,000,000	$20,000,000	$20,000,000	$10,000,000	$10,000,000
Alabama	5,718,784	3,894,298	1,824,486	608,162	608,162	304,081	304,081
Alaska	500,000	200,000	300,000	100,000	100,000	50,000	50,000
Arizona	1,474,342	1,003,978	470,364	156,788	156,788	78,394	78,394
Arkansas	3,440,684	2,342,990	1,097,694	365,898	365,898	182,949	182,949
California	9,329,085	6,352,791	2,976,294	992,098	992,098	496,049	496,049
Colorado	1,774,379	1,208,291	566,088	188,696	188,696	94,348	94,348
Connecticut	1,098,110	747,776	350,334	116,778	116,778	58,389	58,389
Delaware	500,000	200,000	300,000	100,000	100,000	50,000	50,000
District of Columbia	521,277	221,277	300,000	100,000	100,000	50,000	50,000
Florida	5,610,711	3,820,705	1,790,006	596,669	596,669	298,334	298,334
Georgia	6,311,892	4,298,184	2,013,708	671,236	671,236	335,618	335,618
Hawaii	741,182	441,182	300,000	100,000	100,000	50,000	50,000
Idaho	904,333	604,333	300,000	100,000	100,000	50,000	50,000
Illinois	5,920,088	4,031,380	1,888,708	629,569	629,569	314,785	314,785
Indiana	4,647,050	3,164,484	1,482,566	494,189	494,189	247,094	247,094
Iowa	3,128,012	2,130,070	997,942	332,647	332,647	166,324	166,324
Kansas	2,423,351	1,650,221	773,130	257,710	257,710	128,855	128,855
Kentucky	4,920,524	3,350,710	1,569,814	523,271	523,271	261,636	261,636
Louisiana	4,939,940	3,363,932	1,576,008	525,336	525,336	262,668	262,668
Maine	1,297,585	883,611	413,974	137,991	137,991	68,996	68,996
Maryland	2,507,978	1,707,848	800,130	266,710	266,710	133,355	133,355
Massachusetts	3,754,641	2,556,783	1,197,858	399,286	399,286	199,643	199,643
Michigan	6,625,665	4,511,853	2,113,812	704,604	704,604	352,302	352,302
Minnesota	3,831,390	2,609,046	1,222,344	407,448	407,448	203,724	203,724
Mississippi	4,620,857	3,146,647	1,474,210	491,403	491,403	245,702	245,702
Missouri	4,381,818	2,983,870	1,397,948	465,983	465,983	232,991	232,991
Montana	793,320	493,320	300,000	100,000	100,000	50,000	50,000
Nebraska	1,549,077	1,054,869	494,208	164,736	164,736	82,368	82,368
Nevada	500,000	200,000	300,000	100,000	100,000	50,000	50,000
New Hampshire	765,879	465,879	300,000	100,000	100,000	50,000	50,000
New Jersey	3,580,811	2,438,411	1,142,400	380,800	380,800	190,400	190,400
New Mexico	1,237,137	842,449	394,688	131,563	131,563	65,781	65,781
New York	8,975,198	6,111,806	2,863,392	954,464	954,464	477,232	477,232
North Carolina	7,697,764	5,241,916	2,455,848	818,616	818,616	409,308	409,308
North Dakota	957,069	651,731	305,338	101,779	101,779	50,890	50,890
Ohio	7,687,873	5,235,181	2,452,692	817,564	817,564	408,782	408,782
Oklahoma	3,111,526	2,118,844	992,682	330,894	330,894	165,447	165,447
Oregon	1,776,026	1,209,414	566,612	188,871	188,871	94,435	94,435

Pennsylvania	10, 011, 031	6, 817, 173	3, 193, 858	1, 064, 619	1, 064, 619	532, 310	532, 310
Rhode Island	872, 401	572, 401	300, 000	100, 000	100, 000	50, 000	50, 000
South Carolina	4, 451, 971	3, 031, 643	1, 420, 328	473, 443	473, 443	236, 721	236, 721
South Dakota	1, 023, 560	697, 010	326, 550	108, 850	108, 850	54, 425	54, 425
Tennessee	5, 816, 413	3, 960, 781	1, 855, 632	618, 544	618, 544	309, 272	309, 272
Texas	11, 387, 745	7, 754, 669	3, 633, 076	1, 211, 025	1, 211, 025	605, 513	605, 513
Utah	1, 123, 938	765, 364	358, 574	119, 525	119, 525	59, 762	59, 762
Vermont	658, 733	358, 733	300, 000	100, 000	100, 000	50, 000	50, 000
Virginia	5, 127, 141	3, 491, 409	1, 635, 732	545, 244	545, 244	272, 622	272, 622
Washington	2, 468, 046	1, 680, 656	787, 390	262, 463	262, 463	131, 232	131, 232
West Virginia	2, 690, 599	1, 832, 207	858, 392	286, 131	286, 131	143, 065	143, 065
Wisconsin	4, 022, 435	2, 739, 143	1, 283, 292	427, 764	427, 764	213, 882	213, 882
Wyoming	518, 782	218, 782	300, 000	100, 000	100, 000	50, 000	50, 000
Guam	144, 340	98, 290	46, 050	15, 350	15, 350	7, 675	7, 675
Puerto Rico	5, 058, 451	3, 444, 635	1, 613, 816	537, 939	537, 939	268, 969	268, 969
Virgin Islands	69, 056	47, 024	22, 032	7, 344	7, 344	3, 672	3, 672

Basis of allocations, per statutory formula:

(*a*) Total population according to Bureau of the Census 1960 Census of Population Advance Reports: Final Population Counts PC (A1)-1 for States (U.S. summary, dated Nov. 15, 1960). Guam, Puerto Rico, and Virgin Islands based on 1960 census as certified to the Public Health Service by the Bureau of the Census.

(*b*) Allocation percentages for the fiscal years 1962 and 1963, as promulgated in the Federal Register, Sept. 10, 1960. March 1961.

MONDAY, MARCH 20, 1961.

ENVIRONMENTAL HEALTH ACTIVITIES

WITNESSES

DR. ROBERT J. ANDERSON, DEPUTY CHIEF, BUREAU OF STATE SERVICES
VERNON G. MACKENZIE, CHIEF, DIVISION OF AIR POLLUTION
WESLEY E. GILBERTSON, CHIEF, DIVISION OF ENGINEERING SERVICES
DR. HAROLD J. MAGNUSON, CHIEF, DIVISION OF OCCUPATIONAL HEALTH
DR. FRANCIS J. WEBER, CHIEF, DIVISION OF RADIOLOGICAL HEALTH
GORDON E. McCALLUM, CHIEF, DIVISION OF WATER SUPPLY AND POLLUTION
DR. THEODORE J. BAUER, CHIEF, BUREAU OF STATE SERVICES
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	6,009	9,795	12,347
	Positions other than permanent	226	295	368
	Other personnel compensation	36	37	20
	Total personnel compensation	6,271	10,126	12,735
12	Personnel benefits	1,085	1,491	1,870
21	Travel and transportation of persons	906	1,323	1,650
22	Transportation of things	129	222	280
23	Rents, communications, and utilities	248	608	870
24	Printing and reproduction	115	192	249
25	Other services	313	778	963
	Services of other agencies	147	289	504
	Research contracts	1,228	2,634	2,999
	Payments to—			
	"Bureau of State Services management fund"	1,203	1,752	2,001
	"National Institutes of Health management fund"	75	103	136
26	Supplies and materials	472	900	1,051
31	Equipment	949	2,314	2,033
41	Grants, subsidies, and contributions	9,303	12,081	14,519
	Total obligations	22,444	34,813	41,860

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	1,091	1,740	2,176
Full-time equivalent of other positions	38	47	57
Average number of all employees	999	1,574	2,032
Number of employees at end of year	1,182	1,778	2,267
Average GS grade	7.2	7.2	7.1
Average GS salary	$6,047	$6,337	$6,189
Average salary of ungraded positions	$5,245	$4,802	$4,802

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Air pollution control	5, 164	7, 003	8, 100
2. Milk, food, interstate, and community sanitation	3, 114	4, 520	5, 604
3. Occupational health	1, 818	3, 325	3, 981
4. Radiological health	3, 060	7, 432	9, 147
5. Water supply and pollution control:			
(a) Grants to State and interstate agencies	2, 901	3, 000	3, 000
(b) Research and direct operations	6, 013	8, 976	12, 028
Total program costs	22, 070	34, 256	41, 860
6. Relation of costs to obligations: Obligations incurred for costs of other years, net	373	557	------------
Total obligations	22, 444	34, 813	41, 860
Financing:			
Comparative transfers from (—) other accounts	−6, 891	−6, 870	------------
Unobligated balance lapsing	167	------------	------------
New obligational authority	15, 720	27, 943	41, 860
New obligational authority:			
Appropriation	15, 720	27, 640	41, 860
Proposed supplemental due to pay increases	------------	303	------------

GRANTS FOR WASTE TREATMENT WORKS CONSTRUCTION

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
Grants for construction (total costs—obligations) (object class 41)	48, 822	47, 093	50, 000
Financing:			
Unobligated balance brought forward	−9, 099	−7, 093	−5, 000
Unobligated balance carried forward	7, 093	5, 000	5, 000
New obligational authority (appropriation)	46, 816	45, 000	50, 000

Mr. FOGARTY. Dr. Anderson, are you going to justify the request for environmental health?

Dr. ANDERSON. I will try to, sir. Part of it. I have the program directors here.

Mr. FOGARTY. I think we should have an overall statement first and then we will go down the line, just as we did on the community health, and ask everybody to make a statement.

Dr. ANDERSON. That will be fine.

Mr. FOGARTY. Do you have an overall statement to make?

Dr. ANDERSON. Yes, sir, I do.

GENERAL STATEMENT

Dr. ANDERSON. In order to provide a more complete presentation of environmental health programs, each of the activities in this appropriation will be presented by the program directors concerned. These men are: Mr. Vernon Mackenzie for air pollution control; Mr. Wesley Gilbertson for milk, food, interstate and community sanitation; Dr. Harold Magnuson for occupational health; Dr. Francis Weber for radiological health; and Mr. Gordon E. McCallum for water supply and pollution control and waste treatment works construction grants. My remarks will be directed to points general and common to all of these activities.

SPECIAL REPORT AND HEARINGS

Last year, at the request of Congress, the Surgeon General presented a report on environmental health problems which was prepared after consultation with a group of citizens headed by the now special assistant to the Secretary for Health and Medical Affairs, Mr. Boisfeuillet Jones, and extensive hearings were held on this subject. The report and hearings highlighted many important facts about the problems of environment health; among them, I would like to emphasize two.

First, advances in technology and in the quantity of contaminants in the environment have steadily skyrocketed in recent years. As our industrial civilization progresses, more and different contaminants will be produced and introduced into the air and water and food on which we depend for life itself.

Second, like some other disease agents, these technological advances and increased quantity of contaminants are intimately related to man's economic and social growth. This enormously complicates any approach to control of environmental health hazards. Thus, maintaining a healthful environment touches at the core of our industrial, economic, political, and recreational life. For progress, therefore, we need to have the understanding, cooperation, and activity of these groups as well as we need technical biomedical and bioengineering know-how to bring about effective control, if we are to reduce the very real threat posed by our polluted environment. We have sought to have these concerns reflected in our advisory bodies—the National Advisory Committee on Radiation, the Water Pollution Advisory Board, the Air Pollution Advisory Board, and the Committee on Occupational Health. These bodies have set goals, advised on specific activities and levels for specific proposals—the basis for our programs and plans.

At the special hearing on environmental health, the threat to our well-being—and our very existence—was brought out by expert and citizen witnesses. Some of the specific problems, and the serious impact they have on our national health and life, will be discussed by the witnesses who follow me today. At this point, I merely note that, as a nation, we are beginning to be aware of this serious matter confronting us, that it will grow in our future, and that we are now starting to do something about it.

RESEARCH

As we see it, a principal emphasis in environmental health work for many years to come, at least in terms of Federal effort, must be in research—seeking the answers to problems of control. We need more fundamental knowledge, more early experimental work, to work out practical models and methods for the effective control of many hazards.

The complexity of research needed in this area staggers the imagination. In many cases, we are dealing with very low concentrations of substances—for example, perhaps one or 2 parts per billion in water or air—some substance which may be a killer if absorbed by an individual over a longer period of time. The detection of these substances, the measurement of their effect on humans, and the practical problems of removal of these small quantities from water and air—these present research problems of a new order of complexity and difficulty unlike most of those which have been resolved in the past. Similarly, complex problems are present in low-level radiation hazards, in occupational exposures, in milk and food technology. These problems cut across the several programs and make an integrated research approach essential if we are to integrate the effect. For example, a substance may be present in small quantities in water and in air and be in food, so that man's intake is the sum of all. Furthermore, our programs in air and water are working on the effects of pollution on animal, plant, and fish life.

In this great research task, we expect to stimulate and support the work of other scientists and agencies in these fields. Research grants which have worked so well in the medical-biological field are an essential element in the environmental health area. With the cooperative help of the officials of the National Institutes of Health, the funding of research grants in this area is now proposed in the request for the appropriate programs in environmental health activities.

Our principal research laboratories today are in Cincinnati, Ohio, at the Sanitary Engineering Center that houses research and training programs for air, water, engineering, and radiological health, and at the Occupational Health Center. Other research activities are scattered in several locations. We are meeting program space needs in temporary buildings at the SEC site and in rented space. But we remain crowded. The environmental health report identified the need for a central environmental health facility in the Washington area to permit adequate and coordinated emphasis to be given to the intramural and extramural research program in the years ahead and to provide for related training and technical assistance activities. The first steps have been taken for the planning of this center and for seeking a site.

CONTROL

While research must be our main focus for the future, we are not neglecting measures we already have to mitigate and control the present problems of polluted air and water, radiation hazards, occupational disease, and safe handling of food, milk, water, and sewage. Our budget, therefore, includes amounts for training of personnel, technical assistance, construction of waste treatment facilities, and enforcement measures to bring about control of present hazards by State and local agencies and ourselves.

To sum up: The problems of environmental health are being compounded with every day that passes. The need is urgent for catching up in knowledge through research; in personnel through training; and in control through construction grants, technical assistance, and enforcement activities. In the 1962 request, the appropriation "Environmental health activities," provides $41,860,000, an increase of

$7,047,500. The request for waste treatment works construction grants is $50 million.

If there are any general questions, I will try to answer them.

ADEQUACY OF THE 1962 BUDGET

Mr. FOGARTY. You referred to the report and the 2-day hearing we held in this committee last year. We thought we had some pretty good men come in.

Dr. ANDERSON. You did.

Mr. FOGARTY. We asked the Public Health Service then what they thought we ought to be spending. This was last year. I think Dr. Burney said $26 million more. Now all you are coming in here for is just an increase of $7 million. Have you changed your mind as to the $26 million figure?

Dr. ANDERSON. No, sir. We still think that the need for a marked program expansion exists here.

Mr. FOGARTY. I think in direct operations alone it was said that you ought to have $9 million more and you are not asking for half of that. What did you ask the Bureau of the Budget for?

Dr. ANDERSON. The Bureau of the Budget request was for $47,413,000.

Mr. FOGARTY. They cut you over $5 million?

Dr. ANDERSON. Or $6 million.

Mr. FOGARTY. What would that $6 million be used for?

Dr. ANDERSON. That $6 million would have allowed expansion particularly in one field, where very little expansion is allowed, namely, the occupational health field. There is requested only a very small increase in the occupational health program. The other items that we were hoping to expand were air pollution; milk, food, interstate and community sanitation, where we wished to increase our milk sanitation work; the shellfish program and food service sanitation and interstate sanitation. That is the work in connection with airplanes, buses, railroads, and then some addition to our general sanitation training program.

I might say in the air pollution program we had hoped to do more toxicological work on the effects of some of the chemicals that are present in the air.

In occupational health we hoped to expand our laboratory research on toxicology on various substances used in present-day industry. We had hoped to extend some of our epidemiological studies in certain of the large industrial working groups in the country, and we wished to give special assistance to States.

These plans we are not able to implement under this request.

REQUEST FOR BUDGET AMENDMENT

Mr. FOGARTY. Is there any budget amendment for environmental health?

Dr. ANDERSON. Not in the area of program operations, sir. All of these with the exception of occupational health did have increases in direct operations, and there were increases provided for in the research grant program to outside agencies and institutions. So this area of the program did not quite fit the program criteria that were set up.

Mr. Fogarty. Why did it not fit?

Dr. Anderson. Well, Mr. Kelly can explain about increases here.

Mr. Kelly. I think this was an area where the difference between the budget proposal and what has finally been allowed was a matter of degree in this program. As we understood the instructions, it was the kind of thing that should be commenced by the new administration in 1963, rather than by an amendment at this time.

Mr. Fogarty. Even though the report indicated we ought to be spending $26 million more.

Mr. Kelly. Yes.

Mr. Fogarty. So you just want to put it off for a year. Is that right?

Mr. Kelly. This is our understanding of the instructions.

Mr. Fogarty. Some people do not think it ought to wait a year. They think that it is important enough to go ahead now. These people that came before us were all expert in the field, and they seemed to think that we are not keeping up with what we ought to do. Not much is known about some of these problems.

What do you think we ought to be spending?

Dr. Anderson. Well, I think that this has to be an area for increasing program emphasis over the years to come. Each year that we postpone increasing some of these things means we are just going to drop further behind. We had hoped we would increase this by somewhere around $14 million to $15 million more than our 1961 level of activity, excluding the extramural research grants part of the operation.

CONSTRUCTION OF ENVIRONMENTAL HEALTH CENTER

Mr. Fogarty. I was hoping you would ask the Department for more than you did. Did you ask for any funds for a building?

Dr. Anderson. Yes. We have under discussion currently with the Bureau of the Budget a request for an amendment to the 1962 request to provide funds for the purchase of a site and for the architectural and engineering work that needs to be done on the layout. We also have at the National Capital Planning Commission a request for their assistance in determining the final site for the plant which we are proposing. The amendment, as I see it——

Mr. Fogarty. You are asking them to pick a site?

Dr. Anderson. No. They come into the matter of site determination because of their concern with the overall distribution of governmental agencies and operation in the area, as well as the transportation lines, and communication lines, and so on, that must be provided. But we select our first choice and submit it to them for their review.

Mr. Fogarty. Have you made your first choice?

Dr. Anderson. We have indicated to them the site we would prefer. Yes, sir.

Dr. Terry. You also indicated we have other acceptable sites.

Dr. Anderson. Yes.

Mr. Fogarty. When are they going to act?

Dr. Anderson. Their next meeting is in April and it is possible that they will act at that time, although they have asked us for some additional information in connection with another site.

Mr. Fogarty. Who is the first man to explain the programs?

Dr. Anderson. Mr. Mackenzie for the air pollution program.

GENERAL STATEMENT ON AIR POLLUTION

Mr. FOGARTY. All right. Go ahead.

Mr. MACKENZIE. Thank you, Mr. Chairman. I have a statement to file for the record which, with your permission, I would like to summarize orally.

Mr. FOGARTY. All right.

(The statement follows:)

Mr. Chairman and members of the committee, for the past several years, the Public Health Service has been increasingly concerned with the seriousness of the air pollution problems which have arisen as unwelcome byproducts of our industrialized, urbanized, and mobile society. The problems are varied, as are the effects of air pollution and the reactions of the public. We in the Public Health Service get a fairly accurate picture of the range of public concern on air pollution through the many letters we receive from all parts of the country, and increasingly, from many foreign nations. What was once primarily a general annoyance at the dirtiness of smoke has become a matter for concern of a far more serious nature. Economic losses due to air pollution to important segments of our society, including agriculture, are now significant both in national terms and particularly to individuals and business organizations directly and seriously affected to the point of economic insolvency. But the most disturbing concern today is, without doubt, the question of the serious hazards to human health which air pollution presents.

The subcommittee members have heard about the striking disasters such as those in Donora, Pa., and London, England. Given certain meteorological conditions, these types of disasters remain a constant threat. Some progress has been made toward the end of keeping responsible officials better alerted to such possible outbreaks. In Los Angeles, for example, alert plans provide for drastic curtailment of sources of air pollution emissions under stated levels of pollution in the community atmosphere. The Public Health Service and the Weather Bureau have recently instituted a special program of forecasting situations of serious air pollution potential for all portions of the United States, east of the Rocky Mountains.

Of even more concern for the mass of our citizens are the cumulative, chronic health effects of long exposures to polluted atmospheres. More of our people are living longer, more closely packed together in cities, and in increasingly polluted community atmospheres. Research has produced a sufficient amount of incriminating evidence to convince us that there exists a public health problem of major proportions related to air pollution.

We know of the higher incidence of certain pulmonary and cardiac diseases among urban residents as compared to rural residents. Further, within individual cities, similar variations in death rates may be observed to correlate with gross differences in air pollution levels.

Second, we know from laboratory experiments on both animals and human beings that certain pollutants, singly or in combination, adversely affect the ability of the animal or the exposed person to breathe. Also, from laboratory experiments, we know that certain types of air pollutants cause direct damage on respiratory tissues or may interfere with normal physiological protective mechanisms. Thus, animals exposed to certain irritating gases become more susceptible to infection. Assay of the air quality of many American cities shows that substances capable of producing effects of this kind are usually present, although the specific effects associated with the concentrations encountered are not entirely clear within our present status of knowledge.

The job facing us, while difficult and complex, is nevertheless clear. We want to retain the advantages of our industrial and urban society. The Congress has expressed its views in enacting the Air Pollution Research and Technical Assistance Act in 1955; extending it and broadening its authority in 1959; and enacting Public Law 86–493 relating to the study of the effects of automotive emissions on human health. Since 1955, 10 States have enacted legislation on air pollution problems; however, the degree of program followup in support of this type of legislation is quite varied. Spokesmen for the States, such as the Council of State Governments, and organizations representing cities such as the American Municipal Association have emphasized the need for more vigorous activity.

There is much which can be accomplished today, in terms of technical feasibility, which is not being done. But there still exists a considerable gap in technical understanding of the nature, the behavior, the effects, and the means for control of air pollutants. For this reason, the Public Health Service air pollution activity has emphasized research and the 1962 estimates illustrate this special need. Members of the subcommittee may be familiar with the recently issued report "National Goals on Air Pollution Research." This report, prepared by a non-Government advisory group of experts representing diverse segments of our society, has projected air pollution research needs through 1970, recognizing the need for substantially increased activity by the States, by industry, and by the Federal Government. Our 1962 planning, as reflected in the budget estimates, has been guided by this report, within existing statutory and financial limitations. Within the Public Health Service, the recent creation of the Division of Air Pollution provides an improved administrative and organizational basis for an orderly achievement of the goals established in the report.

FISCAL YEAR 1962 PROGRAM

The program in more specific detail is contained in the justification material in the budget documents. Research will continue to receive the greatest emphasis. Two areas of expansion called for in the estimates are in research grants and in the automotive emissions research activity. An increase of $988,400 is requested for fiscal year 1962 to cover expansion of these two areas.

RESEARCH GRANTS

Research grants support fundamental studies, primarily in universities, which produce information upon which subsequent practical control activities can be developed. In the past several years, the research grants portion of the program has produced some important findings. For example, one investigator has demonstrated that the protective ciliary activity in respiratory passages, which is important in removing irritating and damaging contaminants which may lodge there, is reduced or destroyed by exposure to certain air pollutants. Another study has developed procedures whereby airborne particulate pollutants can be characterized and identified by microscopic examination, thus giving practical information as to the sources from which they come and the relative importance of the various types of pollutants which are present.

AUTOMOBILE EXHAUST STUDY

The major area of increase, automotive emissions research, is directly related to the requirements of Public Law 86–493. This act requires the Surgeon General to conduct studies on the amounts and kinds of substances which, from the standpoint of human health, it is safe to discharge from motor vehicles to the atmosphere. A report to the Congress on the results of the study and such recommendations as may be considered appropriate, is required by June 1962, under the terms of the act. During 1961, much of the time and resources available are being used in acquiring the special facilities and equipment required for such research. During 1962, full-year research activity, both in the laboratory and in the field, will be conducted and the report to Congress will be prepared.

Several approaches will be used in a concentrated attack on the several problems relating to the effects of automotive emissions. Animals will be exposed to artificially produced exhaust and its constituents, under carefully controlled conditions. Animals will be exposed to naturally occurring exhaust, near heavily trafficked areas, and analyses will be made of the biological effects. The effects of tetraethyl lead and carbon monoxide on man, currently under study, will be more intensively studied, using special population groups. Emphasis will be given to studies of the effects of 3–4 benzpyrene and other known or suspected carcinogens. An important element in all of these studies will be the collection and analysis of data on levels of automotive emissions in the air of representative cities and their relationship to the general quality of the community atmosphere.

GENERAL GOAL OF THE PROGRAM

Finally, some reference should be made to the total picture of the national air pollution control effort and the manner in which the Federal Government's responsibility fits into this picture. Actual control activities are the responsibility of the States and communities and industry. Our statutory responsibility includes research and technical assistance. In backup of State and local control agencies, we consider it important that our technical findings be disseminated as early as possible and as widely as possible so as to facilitate effective and economical control measures. We also have a sense of urgency that available knowledge be put to use without unwarranted delay—the evidence of our research on health effects gives ample support to this sense of urgency.

There is requested in this budget $8,100,000 for air pollution activities in 1962, an increase of $988,400 over 1961.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Mr. MACKENZIE. I think that the members of this committee are well aware of the air-pollution problem which has arisen as an unwelcome byproduct of our increasingly industrialized, urban, and mobile society. For the past several years we in the Public Health Service have been increasingly concerned about the seriousness of this air-pollution problem. The most disturbing concern, without doubt, is related to the serious hazard to public health which air pollution now presents.

More people are living closely together in our cities, and in increasingly polluted atmospheres. Research has already produced sufficient incriminating evidence to indicate that we have a public health problem of major proportions in relation to air pollution. Much can be done to alleviate this situation in terms of technical feasibility—much more than is actually being done. But there still exists a considerable gap in the technical understanding of the nature, the behavior, the effects and the means of control for specific air pollutants. For this reason the Public Health Service in its program has emphasized research over the past several years, and the 1962 estimates continue this emphasis.

SPECIAL REPORT

During the past 2 years an intensive review has been made of the national needs for air pollution research by an eminently qualified ad hoc group, appointed by the Surgeon General, of non-Federal representatives from various segments of our society. The resultant report——

Mr. FOGARTY. They are going to be very disappointed with this budget too, aren't they?

Mr. MACKENZIE. I might say that the present budget was drawn up prior to the time that this report came out.

Mr. FOGARTY. Well, that does not change my statement.

Mr. MACKENZIE. That is right.

Mr. FOGARTY. Do you not think they will be disappointed?

Mr. MACKENZIE. Yes. I think they may. Certainly this is not fully in accord with the recommendations as they were included in the report.

Mr. FOGARTY. No, it is not.

Mr. MACKENZIE. This report projects the needs, as you may have noted, to the year 1970, and recognizes a need for substantial increase of research in this field by States, by industry, and by the Federal Government.

POLLUTION FROM AUTOMOBILE EXHAUSTS

The 1962 estimates provide for expansion in two areas of research with respect to air pollution. First, increased support for research grants and, second, an increase in our research activities concerned with emissions from automotive vehicles.

Dr. ANDERSON. This is under the Schenck law.

Mr. FOGARTY. I think that the automobile industry and the petroleum industry should be doing a lot more than they are. The petroleum industry got a little bit upset because I didn't think it was doing as much as it should do, which was all right with me. I still do not think it is doing half of what it ought to be doing. I will go into that later on. Go ahead now.

Mr. MACKENZIE. The total increase requested amounts to $988,400 to cover the increased expenditures in these two areas. The major area of increase, that which is related to research on emissions from automotive vehicles, is concerned with the requirements of Public Law 493 as enacted by the last session of the 86th Congress. This act requires the Surgeon General to conduct studies of the amounts and kinds of substances which, from the standpoint of human health, it is safe to discharge from motor vehicles into the atmosphere. A report to the Congress is required by June 1962.

In 1961 we are expanding research on the health effects of automotive emissions; we are initiating the installation of necessary equipment and facilities, and are starting studies in a number of localities. Animals are being exposed to exhaust and its constituents under carefully controlled laboratory conditions. Animals are also being exposed to naturally occurring exhaust in the vicinity of heavily traveled roadways. Examinations will be made of the biological effects which occur from such exposures. Studies of the effects of carbon monoxide and of atmospheric lead on man, currently underway, will be intensified. Emphasis is being given to studies of the extent of contamination by, and the effects of 3-4-benzpyrene and other known or suspected carcinogens. An important ancillary study is concerned with the collection and analysis of data with respect to the variations in the concentration of pollutants associated with automotive emissions in the air of representative cities throughout the country, and the relation of these levels to the general quality of the atmosphere in these locations.

RESPONSIBILITIES OF PHS AND OTHERS

The Public Health Service's statutory responsibility in the air pollution field includes research and technical assistance. The responsibility for air pollution control rests with the States and local governments. In backup of State and local government control agencies we are making a special effort to disseminate new information from research as rapidly as possible and as widely as we find it feasible for us to do. The results of our research on the health effects of air pollutants make it urgent in our opinion that the available knowledge be put to use in controlling air pollution without any unnecessary delay.

The budget request for air pollution activities in 1962 is $8,100,000, an increase of $988,400 over 1961.

Mr. Chairman, I will be glad to answer any questions that you or other members of the committee may have regarding the program or about the budget request.

POLLUTION FROM AUTOMOBILE EXHAUSTS

Mr. Fogarty. Automobile exhaust has been a problem for a long time. I am glad that we are going ahead with some program but I have thought that the Federal Government should not bear the full responsibility, that the automobile industry and the petroleum industry ought to do more of this research. Are you satisfied with the amount of research carried on by those two industries?

Mr. Mackenzie. Mr. Chairman, I personally, from a technical standpoint, cannot be satisfied with the amount of research that is being carried on by any of the parties that have a responsibility for participating in it.

Mr. Fogarty. They will spend $25 million on research trying to develop a higher octane gas, but they will not spend $5 million on trying to refine what comes out of the exhaust pipe.

Mr. Mackenzie. I think that the research on devices has been stepped up in the last couple of years, not exclusively by the automobile industry or the petroleum industry. There are many other segments of industry that now are participating in this particular activity—the chemical industry and others. It may be that there will be a source of income associated with this in the future but we are very glad to see that this type of research has been stepped up.

CALIFORNIA LAW

Mr. Fogarty. Did California pass a law?

Mr. Mackenzie. Yes, sir. The State of California passed a law which will require the installation of devices on automobiles to control emissions within 1 year, on new vehicles, after a State board approves two devices as meeting the requirements of the California act.

Mr. Fogarty. What will they cost?

Mr. Mackenzie. No devices have been certified as yet.

Mr. Fogarty. Not yet?

Mr. Mackenzie. The board which was established by the State law in California is just now becoming operative. They have acquired some laboratory facilities for test purposes and have a staff, and are in the process of outlining the criteria and requirements for submission of devices for test appraisal.

Mr. Fogarty. I thought some one told us last year that some of this equipment cost around $35.

Mr. Mackenzie. There are two types of devices that have been worked on as applying to automobiles. One of them is quite inexpensive—that which relates to the control of emissions from crankcase ventilation. The emission from this source may run perhaps 25 to 30 percent of what comes from the vehicle in all. The automobile industry is currently providing these devices on all vehicles which are sold new in California this year. They are available on individual order to other purchasers, installed as factory equipment at a cost which generally runs from $3.50 to about $5.50. The more expensive type of device is for the control of emissions in the exhaust of a vehicle, and here only tentative estimates are available. There have been estimates that these might cost anywhere from $35 to perhaps $150. There are none that are currently on the market.

Mr. FOGARTY. I see. Is California the only State that has such a law?

Mr. MACKENZIE. Yes, sir.

DONORA INCIDENT

Mr. FOGARTY. This has been a serious situation in air pollution for a long time. I remember the first time it was brought to our attention was 13 or 14 years ago by the Donora, Pa., incident.

Mr. MACKENZIE. Yes, sir. Donora, Pa.

Mr. FOGARTY. That was a serious one.

Mr. MACKENZIE. An acute episode. I think aside from the acute episodes like Donora, however, where we know that people can be made acutely ill, or even die, one of our major concerns is the long-term effect on people of exposure to low-level concentrations day after day and year after year. The results of our research are indicating reasons why we should be more urgently concerned about this latter aspect of health effects from air pollutants.

Mr. FOGARTY. I think about 20 persons died at Donora. There was a followup study made by the Public Health Service, wasn't there?

Mr. MACKENZIE. Yes, sir.

Mr. FOGARTY. Are you familiar with that study?

Mr. MACKENZIE. Yes, I am in general.

Mr. FOGARTY. Did you gain anything from it?

Mr. MACKENZIE. Well, in general the results of the restudy of the people living in Donora showed that those who had been affected at the time of the acute episode apparently had a less favorable prognosis with respect to illness than other people in the general population.

Mr. FOGARTY. This headline from a year or two ago said, "Survivors of 1948 Poison Fog at Donora Show an Increased Death Rate."

Mr. MACKENZIE. Yes, sir.

Mr. FOGARTY. Is that borne out by your study?

Mr. MACKENZIE. By the study. Yes, sir.

ADEQUACY OF 1962 BUDGET

Mr. FOGARTY. This increase of $900,000 is not much of an increase in comparison with your "national goals in air pollution research," is it?

Mr. MACKENZIE. I think there is nothing that we are including in the 1962 estimates that would be inconsistent with the goals report, although from the standpoint of budget magnitude it does not fully implement the recommendations of the report.

Mr. FOGARTY. Which report are you referring to?

Mr. MACKENZIE. The National Goals Report.

Mr. FOGARTY. That is the ad hoc committee of the Surgeon General?

Mr. MACKENZIE. Yes.

Mr. FOGARTY. How does it compare with the report to this committee at the hearing that was held last year?

Mr. MACKENZIE. We have not reached that level, sir.

Mr. FOGARTY. You are a long ways from it. Do you think you will ever reach it at the rate you are going? I am not blaming you. You are not to blame for it.

Mr. MACKENZIE. Well, President Kennedy, in his message on resources to the Congress gave some degree of emphasis to the urgency for increasing Federal activity in this area as well as others.

PROPOSED BUDGET AMENDMENT

Mr. FOGARTY. That is why I thought there would be a budget amendment, but we do not have one. Did you request a budget amendment or were you told not to ask for one?

Mr. MACKENZIE. There was none transmitted from the Department to the Bureau of the Budget.

Mr. FOGARTY. Were you told not to submit one or were you just given a hint that it would not do any good to submit one?

Mr. ACKERMAN. There were internal proposals developed that were discussed, and these criteria were applied to the various proposals.

Mr. FOGARTY. Did you have any proposal in mind in case you had been asked?

Mr. MACKENZIE. Yes, sir.

Mr. FOGARTY. What was it?

Mr. MACKENZIE. We prepared a possible amendment to the budget amounting to $1,724,000.

Mr. FOGARTY. That is a very modest request.

Mr. MACKENZIE. This provided an increase for two items.

Mr. FOGARTY. Will you break that down for the record?

Mr. MACKENZIE. I will be glad to, sir.

Mr. FOGARTY. And how it would be used.

Mr. MACKENZIE. Yes, sir.

(The information requested follows:)

EXPLANATION OF PROPOSED AMENDMENT TO 1962 ESTIMATES FOR AIR POLLUTION

Total additional amount proposed, $1,724,000

PROJECTS

Automotive exhaust activities under the Auto Exhaust Research Act (Schenck Act) of 1960, $524,000

The act, signed on June 8, 1960, provides for an accelerated research activity on the health effects of automotive emissions and a report thereon to be submitted to Congress at the end of 1962. The 1962 budget provides funds to implement this legislation. An increase of $224,000 would permit the development of research data in greater depth for inclusion in the report to Congress due June 30, 1962.

The expanded activities undertaken under the Schenck Act have required additional laboratory space. The 1962 estimates were prepared and presented to Congress on the basis that, in 1962, leased space would be financed by the General Services Administration. We were subsequently informed that funds were not made available to GSA and therefore they would be unable to provide such financing in 1962. For this reason $300,000 for rental and maintenance costs of the special laboratory building in Cincinnati, Ohio, would have to be diverted from research funds if the budget were not amended as proposed.

Research grants, $1,200,000

The use of additional funds to support the growing volume of approved research projects in universities is discussed in the narrative describing the increase of $4,745,000 as requested in the preliminary estimate for 1962 described under research grants on page 241.

ORIGINAL 1962 ESTIMATE

Mr. Fogarty. What was your original estimate?

Mr. Mackenzie. The original estimates we made in this area amount to $12,845,000.

Mr. Fogarty. Compared to what?

Mr. Mackenzie. The budget allowance that is currently before you is $8,100,000.

Mr. Fogarty. That is $4,700,000, difference. You are short about $4,700,000. I think you had better give us a breakdown of the $4,700,000—what it would be used for, and why you thought it was important.

Mr. Mackenzie. Yes, sir.

(The information requested follows:)

Planned uses for additional $4,745,000, as included in the preliminary 1962 estimates for air pollution activities

Program activity	Positions	Preliminary estimate	Positions	President's budget	Positions	Decreases
Grants	--------	$4,657,000	--------	$1,957,000	--------	$2,700,000
Research	--------	2,844,000	--------	1,844,000	--------	1,000,000
Training	--------	813,000	--------	113,000	--------	700,000
Surveys and studies	--------	1,000,000	--------	--------------	--------	1,000,000
Operations	442	8,188,000	382	6,143,000	60	2,045,000
Research	352	7,106,000	326	5,477.600	26	1,628,400
Technical assistance	61	789,500	39	429,900	22	359,600
Training	29	292,500	17	235,500	12	57,000
Total requests	442	12,845,000	382	8,100,000	60	4,745,000

1. GRANTS

Research grants, $1 million

The results of fundamental research, supported by research grants, are an important and integral part of the air pollution program, serving as a foundation for practical advances in the understanding and control of air pollution. The research grant mechanism has been effective in stimulating competent scientists to enter this field and has resulted in a significant number of new and important findings related to both the medical and environmental aspects of the problem.

In 1961, the National Advisory Health Council has already recommended to the Surgeon General the approval of more air pollution research grant applications than available funds will support. The estimated backlog of $400,000 existing at the end of 1961 plus anticipated recommended projects in 1962 would require an estimated total of $3 million for support. The formal budget submission includes $1,844,000 for this purpose. The additional $1 million proposed for 1962, as tabulated above, would be applied to additional grant awards.

Training grants, $700,000

A serious obstacle to the achievement of more rapid progress in effective air pollution control is the critical shortage of properly trained specialists. Such specialists are needed by all levels of government and industry, and it is estimated that during the next 10 years about 4,000 such individuals will be needed. The development of local and State control programs, the conduct of surveys assisted by grants-in-aid, and the growth of the problem itself, all serve to accentuate this need.

The present level of the training grant activity, for which no increase is provided in the estimates as submitted, is supporting grants to 10 universities for curriculum support and approximately 6 students by direct traineeships. In view of the growing need for trained personnel, the present level of support for training is not adequate to make any substantial or significant progress in meeting this need. Developing specialized graduate level training resources cannot be accomplished overnight and we therefore consider it important that increased emphasis be placed on this activity if we are to avoid a situation where an effective effort in air pollution control by all levels of government and by industry, is to be seriously hampered for lack of personnel.

Survey grants, $1 million

One of the most urgent needs in the air pollution control field is for the expansion of State and local air pollution control programs. Technical procedures are available for the prevention of most air pollutant emissions; these procedures, however, are not being applied to the extent that is feasible and desirable.

About 6,500 communities, containing about 90 percent of our urban population, have air pollution problems requiring control activities which are recognized to be the responsibility of the States and local governments. Only about 50 percent of these areas have any air pollution control activities at present, leaving a significant portion of our population unprotected. On the State government level, only 15 States now have active air pollution control programs employing full-time personnel.

In each area, a careful survey and appraisal of the problem in the district affected is fundamental to the rational development of a control program, whether on a local, regional, or State basis. The 86th Congress amended Public Law 84–159 to make clear the authority of the Surgeon General to make grants to States and local governments for "surveys and studies" needed for this purpose. The additional $1 million for survey grants proposed for 1962 would provide needed financial assistance to States and local communities and furnish needed stimulation toward the initiation and improvement of organized programs for air pollution control.

2. OPERATIONS

Research, $1,628,400

The additional amounts for intramural research, together with that requested for research grants, above the formal appropriation request, would substantially implement on an orderly schedule the recommendations of the ad hoc advisory group which prepared the report "National Goals in Air Pollution Research." These funds would be used for (1) substantially increased activities concerned with appraisal of the effects of air pollutants on man through both field and laboratory studies, (2) expansion of the present minimal activity concerned with the appraisal of damage to agricultural plants and animals, and the mechanisms by which such damage is caused, (3) implementation of a broader activity concerned with the measurement and identification of chemical contaminants in urban atmospheres and the reactions which occur among them, and (4) an initiation of studies of economic losses to our society caused by air pollution and of the organizational methods for achieving control on State and local government levels.

Within the expanded research program which these additional funds would provide, the major expenditures would be devoted to research on the effects of air pollutants on man and on plants and animals. The following examples are illustrative:

The circumstantial evidence linking air pollution to effects on human health has now built up to the extent that it appears imperative to follow up, with minimum delay, the leads which have now been developed. The recent laboratory breakthrough by which typical lung cancer has been produced in laboratory animals by inhalation exposure to irritant gaseous pollutants opens a number of promising avenues of study which should be exploited as soon as is feasible. In addition to the need for broadened studies of the health effects of ozone, sulfur oxides, and various types of automotive emissions, it has become clear that intensive study will be required of the health effects of the various oxides of nitrogen, which are common to all polluted urban atmospheres and which are capable of producing adverse effects, either singly or in combination with other substances. Pollution from oxides of nitrogen emissions have been demonstrated to be on the increase and have reached levels in some areas which are of health concern. Available information as to their physiological effects is incomplete and conflicting.

Damage to agricultural and ornamental plants and to animals from air pollution has now reached the stage where it can be recognized in all metropolitan areas and in the majority of the States. On the basis of preliminary surveys, such damage nationally is estimated to amount to $500 million annually. At the present time, practically no Federal resources are being devoted to needed research on these problems. Information which would derive from such research is critically needed to provide a rational basis for control activities which would minimize the damage now being produced.

Technical assistance and training, $416,600

The additional funds for technical assistance and training activities ($416,600), above the formal budget for 1962, would assist materially in accelerating the application of new research knowledge in the control of air pollution and in the development and improvement of needed State and local control programs. With a high priority necessarily given to research in the overall program, the air pollution technical assistance activities have been carried on in a highly selective and limited manner to date. The increased urgency of development for more effective control programs on State and local levels, based upon research findings over the past several years, and expansion of Federal stimulation to control activities have assumed new importance. The expansion of technical assistance activities would complement an expanded State and local survey program, as proposed under the survey grants activities. The existing level of resources for technical assistance is not adequate for effective aid to any substantially increased level of State and local control activities.

Expansion of short-term direct training activities in the air pollution field is also aimed at meeting the needs of increased State and local programs. It is particularly important that such short-term training be expanded to provide special orientation in various technical subjects to existing personnel until such time as longer term university training can produce the trained specialists required over the next decade. The expanded short-term training, as proposed, would be especially directed toward enlarged coverage of field training courses to be held in various highly populated areas of the country.

RESEARCH GRANTS

Mr. FOGARTY. Of this small increase you have here, $316,000 is for research grants. In general, what type of research is carried out through grants, and to whom are these grants made? You may give us a couple of examples at the same time.

Mr. MACKENZIE. Yes, sir. Research grants in the air pollution field have been operative for approximately 5 years, since the inception of the air pollution program. Chart A here shows the experience with these grants over the past several years, and the estimates for fiscal 1961 and 1962. The research which is supported by these grants is primarily carried on by universities or the several departments of the universities, that is, engineering, chemistry, physics, medical, biochemical and others. A few of the results of these studies I think may be of interest to you.

I might, by the way, say that in our experience these grants have been very productive in contributing to the overall research value of the program. In the past year, for example, one research grant project has indicated an enhanced susceptibility to respiratory infection on the part of laboratory animals which have been preexposed to certain types of irritant gaseous pollutants. We feel that this is significant and it ties in with another type of study which has indicated an interference by these same types of gaseous pollutants with an important protective body mechanism in the respiratory system. I refer to the action of the cilia which line the respiratory tract and sweep out mucus, and so forth, and by this action protect against infectious agents and other foreign materials entering the respiratory system. So this enhancement of susceptibility to infection ties in with the other findings that certain irritant gases interfere with this ciliary action.

Another study within the last year, which was conducted in a completely different field, is related to the development of methods for microscopic examination of atmospheric solid pollutants to identify the sources from which these came. An atlas for this purpose is currently being prepared which will be of material value to control agencies in identifying substances which they collect in sampling their own individual atmospheres.

Another item which has not yet been reported, but which I think is of major significance, has been told to us by one of the research grant investigators just this last week. He has produced experimental lung cancer in laboratory animals by the inhalation route, using no other artificial method of producing typical metasta sizing cancer than through the exposure to irritant materials by inhalation.

In the long run such results, contributed by the research grants portion of the overall program, will be very significant.

Mr. Fogarty. Do they have more lung cancer in areas with air-pollution problems?

Mr. Mackenzie. I am not familiar with those statistics. I will be glad to get them and submit them.

Mr. Fogarty. No; I will ask the Cancer Institute.

Dr. Anderson. Cancer rates in the large cities are in excess of those in the country generally.

EMPHYSEMA

Mr. Mackenzie. We have been carrying on studies on the health effects of air pollution using a variety of approaches. One of the simplest methods used initially was the comparison of statistics for various sections of the country, and particularly comparisons between urban and rural areas. One example of this type of approach is concerned with the rates for emphysema in males in the United States comparing urban and rural areas which shows it much higher in metropolitan areas.

Mr. Fogarty. What is that?

Mr. Mackenzie. Emphysema is a serious lung disease in which the individual has difficulty in obtaining an adequate supply of oxygen within the lung because too much air is retained in the lung. The lung tissue becomes relatively spongy and the air cannot be expelled. The same disease is showing an increased incidence timewise.

Mr. Fogarty. What happens to a person when he gets that?

Mr. Mackenzie. His physical capability is greatly reduced. He is unable to breathe in the quantities of air that would be required for severe exercise, and to obtain the amounts of oxygen that are required to support such activity. It is a serious disease.

Mr. Fogarty. Do they die from it?

Mr. Mackenzie. Often not from emphysema, as such, although they may be diagnosed as dying from this cause in some instances. In many cases the direct cause of death may be cardiac failure. I would prefer to defer further answer to that question to one of my medical colleagues, sir.

Dr. Anderson. Cardiac problems complicate this condition, as well as infections. In the influenza epidemics, for example, these people who have emphysema have very serious complications because their respiratory reserve is so low. They cannot give up to an infection the little lung tissue they still have for the purpose of getting oxygen into their bodies.

AUTOMOBILE EXHAUST STUDIES UNDER THE SCHENCK ACT

Mr. FOGARTY. Are you going to be able to finish this work on auto exhaust, specified under the Schenck Act last year?

Mr. MACKENZIE. We are confident that we will make significant progress and that we will have items that will be significant to report to the Congress within the 2-year period specified in the law.

Mr. FOGARTY. It is 2 years; is it?

Mr. MACKENZIE. I think there is no question, however, that there are a number of studies that will require a longer term than the 2 years specified in the act, and for which final results could not be obtained in that period.

Mr. FOGARTY. Most of your increase is going to this program. Is that right?

Mr. MACKENZIE. Yes, sir.

NASHVILLE STUDIES

Mr. FOGARTY. What are you doing in your study down at Nashville?

Mr. MACKENZIE. We conducted an epidemiological and environmental study in Nashville, the results of which are currently under analysis. We collected information about morbidity in the population of Nashville, and observed continuously individuals who had specific ailments in an attempt to correlate the variations in responses both in general morbidity and to individuals with chronic disease, to variations in air pollutant levels. We ran this study for approximately a year. One result, shown on chart D, may be of interest to you. This shows the response of individuals in Nashville who are subject to asthmatic attacks during the period July 1958 to July 1959. The response of a number of such patients was kept under continuous observation and this chart shows the correlation of the attack rates with the levels of air pollution as measured by oxides of sulfur. The higher the pollution level the greater was the attack rate in the individuals who are susceptible to asthma.

AGRICULTURAL RESEARCH

Mr. FOGARTY. Are you doing any research in agriculture?

Mr. MACKENZIE. A small amount, sir. We have a small group from the Department of Agriculture on assignment to the Public Health Service at the Sanitary Engineering Center. We are reimbursing the Department of Agriculture for this. The work at the center is of essentially two types: First, research on the use of plants as indicators of pollution; and, second, observation of the effects on sensitive plants of automobile exhaust which is being produced in our test facility there.

NEED FOR REGIONAL PROGRAMS

Mr. FOGARTY. Enforcement of local statutes is difficult, unless you have a regional agreement of some kind.

Mr. MACKENZIE. We have felt, and I think experts in the field have felt generally, that the organization of an air pollution program would be best tied in to the total local or regional area which is affected in each individual instance. Certainly it is impossible to confine air pollution problems to specific local government boundaries in many places like metropolitan areas. In some localities regional programs have been set up which cover the area of concern. In California, for instance, this has been done in the San Francisco Bay area, and also in the vicinity of Los Angeles.

Mr. FOGARTY. We have a good program in Providence, R.I. It was enforced, and it has worked out very well. It is my understanding that, to have it work better, it ought to be on a regional basis and cover a regional area.

Mr. MACKENZIE. Yes, sir. There are many places like that.

Mr. FOGARTY. Thank you very much. Who is next?

MILK, FOOD, INTERSTATE AND COMMUNITY SANITATION ACTIVITIES

Dr. ANDERSON. Mr. Wesley E. Gilbertson, Chief of the Division of Engineering Services covering the milk, food, interstate and community sanitation activity.

Mr. FOGARTY. Go ahead, Mr. Gilbertson.

Mr. GILBERTSON. Mr. Chairman, I have a statement to file for the record, and a short summary which I will read.

(The statement follows:)

STATEMENT BY CHIEF, DIVISION OF ENGINEERING SERVICES ON MILK, FOOD, INTERSTATE, AND COMMUNITY SANITATION

Mr. Chairman and members of the committee; the activity "Milk, Food, Interstate, and Community Sanitation" provides funds for certain basic environmental health activities of the Public Health Service that are essential in the protection of the public health.

Prevention of health hazards due to milk, shellfish, and food services continues to become increasingly complex with rapidly changing technology and new patterns of distribution of industry and the consuming population, and therefore, is more dependent than ever upon the backup that the Public Health Service can give the day-to-day control efforts of State and local health agencies. Through the interstate sanitation program, the Public Health Service discharges its statutory responsibilities under the interstate quarantine regulations in relation to sanitary measures for protection of the traveling public aboard interstate conveyances, including water supply, food service, and waste disposal. The program on environmental health aspects of metropolitan planning and development is emerging as a new and vital activity through which national approaches—both technical and administrative—can be developed on troublesome urban hygiene problems. Under this activity the services also conducts a wide range of technical services on such sanitation areas as: collection and disposal of refuse and solid wastes, plumbing, swimming pools, parks and recreational facilities, trailer courts, and rural and urban sanitation.

We are currently reviewing and evaluating in considerable depth the activities of the Public Health Service in these program areas in connection with the organization studies in the Service. For this reason the programs and related funds encompassed here are, in effect in a transitional stage. However, our studies show clearly the need to focus more emphasis on many problems which are plaguing local urban and metropolitan agencies. In the rapidly growing and coalescing metropolitan areas, basic environmental problems are compounded by unhealthful housing and inadequate recreational areas, by health problems related to land use, lack of planning for health aspects of needed facilities in surrounding suburbs, and other factors of urban life. These environmental problems recognize no political boundaries, yet most metropolitan areas encompass numerous units of local government with different, often conflicting, laws and regulations for coping with environmental problems.

It is well recognized that, although there is still a great deal to learn, we already possess more technical knowledge about environmental factors than we are applying successfully to the urban setting. The immense and increasing environmental problems of the urban area have been brought about by technological advance and demographic trends. Our social, political, legal, and economic structures have not kept pace with these factors of change. Except to a minor degree, our current programs have concentrated upon finding technical solutions and have not given sufficient attention to finding ways to apply this knowledge within a social, political, economic, and legal framework. Yet these are the roadblocks that prevent or control environmental change. To the extent possible within this request, our efforts will be guided in the direction of improving Public Health Service services to the community level.

The public health agencies of our Nation have recognized the challenge of developing a comprehensive approach for the health aspects of the environment. Research, leadership, and technical support should come from the Federal level with the State and local agencies carrying the operational aspects of the programs.

This activity also provides funds for the research grant program in environmental health related to the categorical program areas and for training professional personnel of State and local agencies to keep pace with problems arising from changes in technology.

RESEARCH GRANTS

The funds requested will be used to support research by universities and other nonprofit research institutions on the dangers to health stemming from our environment. The material benefits and social changes deriving from our technological advances frequently are accompanied by new hazards inherent in chemical processes, population growth and concentration, and urban sprawl. Grants will be used to support research concerned with the categorical subjects in this line item and with certain other emerging environmental health factors, including studies of (1) effects of chemical, physical, and biological factors on the safety healthfulness, nutritive quality, and acceptability of milk, shellfish, and other foods; (2) problems of sanitation facilities in homes, institutions, and on interstate carriers; (3) new techniques and approaches on planning for sanitation utilities in metropolitan complexes; (4) ecology, etiology, and epidemiology of food borne diseases, including diseases of food producing animals which may affect their suitability for food usage; (5) disposal of refuse and solid wastes; (6) health aspects of housing including domestic dwellings, schools, and other institutions, hotels, motels, and recreational facilities; and (7) administration of environmental sanitation programs.

The request for $3,310,000 for research grants and for $80,000 for review and approval of grants, will provide for continuance of projects now supported by the National Institutes of Health and will permit growth commensurate with previous experience in extramural research in the above problem areas.

MILK, SHELLFISH, AND FOOD-SERVICE SANITATION

One of the fundamental environmental health programs is the Service's activities to insure that only safe milk, shellfish, and prepared foods are served to the public. While great strides have been made toward the protection of these foods from contamination with disease-producing organisms, developments in food service, including processing and merchandising, have made the task increasingly complex. Milkborne and foodborne illnesses continue to occur in disturbing numbers. It is reliably estimated that more than 1 million cases of foodborne illnesses, including food poisoning, now occur annually in the United States. Available data show that in most instances contamination of food occurred during the final preparation before being served to the public.

Because of changing technology, new environmental factors are being introduced which adversely affect the safety of our milk and food supplies. Chemical and microbiological contaminants are presently increasing hazards. In addition, developments such as ultrahigh temperature pasteurization of milk, pollution of shellfish-growing waters, extension of areas in which paralytic shellfish poison is found, the sale of potentially hazardous foods through automatic vending machines, and the increasing incidence of staphylococcal food poisoning, are a few examples of the types of problems on which State and local public health authorities are requesting assistance from the Public Health Service. These developments are presenting a host of new and complex problems to State and local health agencies. Many are of such nature that they require reappraisal and modification of existing food sanitation practices and procedures. In some instances the very basis of food protection control is changing. State and local health departments do not have the resources to cope with these new problems and, as a consequence, are increasing their demands for Public Health Service assistance.

Our current program in this area is designed to assist States, municipalities, and industry to cope with these problems which, though local in nature, have nationwide scope and impact. The functional activities conducted are (*a*) research and field studies; (*b*) development of new methodology, program guides, and technical procedures: (*c*) provision of consultative services to States, municipalities, and industry on technical problems; (*d*) leadership in the development of standards for the sanitary design and construction of milk and food equipment in cooperation with national health organizations and industry groups; and (*e*) conduct of the cooperative Federal-State programs for the certification of the sanitary quality of milk and shellfish shipped interstate.

In the recognition of the problems in this area of environmental health, the Congress in appropriating funds for 1960 and 1961 directed an increase of emphasis on Public Health Service activities in connection with milk, shellfish, and food-service sanitation, particularly in the areas of research and interstate milk and shellfish certification. In accordance with these directives, Service activities have been reoriented to strengthen, to the extent of available resources, certain research phases of the program and to maintain the cooperative interstate milk and shellfish certification activities at less hazardous operational levels. In 1962, emphasis will be given to (1) field studies to determine if present bacterial standards are adequate in light of present-day methods of handling and processing milk, and of transporting milk over long distances; (2) development and field trial of new technical procedures and administrative practices to replace those which have become ineffective or obsolete due to changing technology in milk sanitation; and (3) field trials and demonstrations of the sanitary provisions and administrative practices of the new PHS model food-service sanitation manual. Seminars for State and local officials will also be conducted to expedite application of new control measures recommended by the Service.

INTERSTATE AND COMMUNITY SANITATION

Certification: Sanitation of interstate carriers

1. *Water supply and food sources.*—The responsibility of safeguarding the drinking water and food consumed by some 2 million interstate travelers each day is carried out by the Public Health Service under the interstate quarantine regulations. This continuing program of inspection and surveillance has been strengthened somewhat recently in accordance with directives of the House. As a result, a greater number of inspections has been accomplished on the vessels, aircraft, dining cars, and buses themselves, as well as on their sources of food and drinking water and their waste handling and disposal methods. In addition to the basic sanitation involved, the program operations have had unique collateral benefits. In several instances, long-needed improvements in public water supply treatment and distribution systems have been obtained because local officials were unwilling to see their public water supply prohibited for interstate carrier use. During the past year the Public Health Service provided additional protection to the public water supplies serving about 5 million persons in the Great Lakes area by delimiting the discharge of vessel wastes in the vicinity of the water supply intakes. This is of importance with the growing traffic since the opening of the St. Lawrence Seaway.

2. *Community environmental engineering problems.*—One specialized area of the Service's responsibility to improve community environment concerns the disposal of refuse and solid wastes. By resolution of the American Public Works Association, public works officials of the Nation have requested the Public Health Service to strengthen its current minimal activities on solid wastes disposal methodology. Even limited field observation has demonstrated glaring

inadequacies in current solid waste collection and disposal practices in the majority of our cities and towns. Again, a small amount of national guidance in the application of the latest and most effective techniques would be helpful in finding solutions to the health and economic problems involved. We propose to initiate practical studies from which to formulate needed criteria, including standards with which to appraise and improve evaluation techniques for solid wastes programs at the local level. We would supplement these activities by providing limited short-term consultation services as requested. Swimming pool standards and practices are being advanced through Service participation in such groups as the Joint Committee on Swimming Pools and the American Public Health Association. A suggested ordinance and regulations covering public swimming pools is under preparation by the Service. In the area of trailer park sanitation a manual, "Mobile House Park Sanitation," was recently prepared by the Service in cooperation with the Mobile Homes Manufacturers Association. This publication incorporates the most modern thinking in design, construction, and operation of mobile home facilities for the guidance of the industry and park operators. In the area of institutional and school sanitation, the National Education Association is currently considering a manual on school environmental engineering to be prepared by the Service and to be issued jointly with the U.S. Office of Education. Greater attention should be devoted to this important facet of institutional environmental health.

ENVIRONMENTAL HEALTH PROBLEMS OF METROPOLITAN PLANNING AND DEVELOPMENT

With two-thirds of our population in metropolitan areas and with community services dependent on a patchwork of multitudinous agencies, there is need for developing effective, comprehensive approaches to the many and varied environmental health problems of metropolitan areas. There is also a pressing need to incorporate health considerations and health competencies in solving the problems of metropolitan development and planning. We must find a way to use the experience gained from the problem situations encountered in a variety of local communities. A number of State and local groups have voiced criticism of the Service for not furnishing such guidance. The National Advisory Health Council and the Association of State and Territorial Health Officers have urged that this type of activity be developed and supported.

In our program, a basic unit of very limited size has been assembling and evaluating information on public health problem relationships to the economic, political science, social, and legal aspects of community organization. Already some tangible results have become available in terms of a community sanitation evaluation guide, which has been used in six metropolitan areas, and technical assistance and consultation to several additional communities.

Requests for assistance in this field from State and local agencies indicate the vital need for greater emphasis on this type of broad attack on the stubborn problems of urban areas. The concept of operation involves a comprehensive approach which stresses the "how" instead of the "what." The "what" related to various environmental problems is derived from technical categorical programs. The approach of the metropolitan planning and the development program is designed to augment these specifics by finding out and showing how individual health needs can be fitted into the community capabilities.

TRAINING

In fiscal year 1961 training courses were initiated on an emergency basis on antibiotics, pesticides, and other chemicals in milk supplies. There is an urgent need for expanding technical training in these areas to equip professional personnel of Federal, State, and local agencies with the knowledge and skills required to cope with new technology. The increase requested will permit specialized training courses to cover neglected areas such as (*a*) training in sampling and analytical methods for measurements of physical, biological, and chemical contamination in milk and other foods; (*b*) special training for laboratory survey officers responsible for certification of milk laboratories; (*c*) expansion of training courses on antibiotics, pesticide residues in milk and other foods; (*d*) initiation of new courses on the detection and control of staphylococci toxin in foods (food poisoning); and (*e*) improved administration of comprehensive environmental sanitation in relation to urban development. These courses for which there has been the most urgent demands from State and local agencies will be given the highest priority, consistent with the nature and extent of research progress in these environmental health areas.

In conclusion, the estimate for this activity totals $5,604,000, an increase of $1,056,900 over fiscal year 1961. Of this increase, the major portion, $762,000 will be directed toward the research grant program, $63,900 to expand our training activities, and the remainder, $231,000, for interstate milk and food and community sanitation activities.

Mr. Chairman, I shall be glad to answer any questions you may have concerning this program and the budget request.

Mr. Chairman and members of the committee, our activity "Milk, food, interstate, and community sanitation" relates to a group of environmental health problems which are of particular interest and concern to local health agencies.

MILK, FOOD, AND SHELLFISH

Rapidly changing methods used in the milk, food, and shellfish industries make prevention of health hazards more difficult. The consuming public is therefore more dependent than ever upon the backup that the Public Health Service can give to the day-to-day control efforts of State and local agencies.

We have made progress, Mr. Chairman, in carrying out the directives of your committee in the 1960 and 1961 reports, which called for increased emphasis on our programs for milk, shellfish, and food service sanitation. Urgently needed research projects have been initiated and Federal participation in the cooperative interstate milk and shellfish certification systems has been strengthened. As before, we have continued to enjoy excellent cooperation from the milk, shellfish, and food service industries.

The food industry is one of the Nation's largest activities—and it is dynamic. Because of changing technology, new environmental factors are being introduced which may adversely affect the safety of our milk and food supplies. Chemical and microbiological contaminants are presenting increasing hazards. Existing and longstanding milk and food health protection practices require reappraisal and modification to suit newer processes and problems. A few examples of developments now facing State and local authorities are: Increased incidence of foodborne infections and food poisoning; more areas in which paralytic poison is found in shellfish; new milk processing techniques, including new methods of pasteurization; increasing pollution of our shellfish-growing waters (very bad in some areas); and the sale of foods which are good media for bacteria growth. State and local health departments find it difficult to cope with these problems and as a consequence, are increasing their demands for our assistance through research and technical consultation.

INTERSTATE CARRIER SANITATION—CERTIFICATION OF PUBLIC WATER SUPPLY AND FOOD SOURCES

The job of safeguarding the health of some 2 million interstate travelers each day is carried out by the Public Health Service in the discharge of its statutory responsibilities under the interstate quarantine regulations. These provide for sanitary control of water supply, food service, and waste disposal used by interstate conveyances. As requested by your committee, this continuing program of inspection and surveillance has been strengthened. We are now giving more emphasis to inspections of vessels, aircraft, dining cars, and buses, their sources of food and drinking water, and their waste handling and disposal methods.

As we carry out our control work under the interstate quarantine regulations, a number of unique collateral benefits are achieved. Improvements in public water supplies have been made by localities both at treatment plants and in distribution systems, fortunately, because local officials do not wish to have the Service withdraw certification of their public supply for interstate carrier use. Currently, the interstate carrier watering point certification program covers purification plants and distribution systems in over 800 cities, located in every part of the Nation, supplying drinking water to more than 120 million citizens. We conduct the certification program in close cooperation with State agencies. Our drinking water testing program provides also an intelligence system by which the microbiological and the changing chemical quality of the drinking water supply of a large part of the Nation can be determined and monitored. In cooperation with other components of the Service, we are now using information from this sampling network in some highly promising research studies on the relationships between water quality and the incidence of certain diseases.

Two-thirds of our population now live in urban areas—and the concentration continues to grow. It has been said that "of all living animals, man is the only one who befouls his own nest." In a majority of these sprawling metropolitan areas, basic environmental and sanitation problems are compounded by unhealthful housing and unsatisfactory recreational areas; by health problems related to improper land use, and lack of planning for growth of surrounding suburbs. These environmental problems recognize no political boundaries. Yet most metropolitan areas encompass numerous local jurisdictions with different, often conflicting, laws, regulations, and administrative mechanisms.

There is need for developing effective, comprehensive approaches to the many and varied environmental health problems of metropolitan areas. Health considerations and health competencies must be brought to bear on environmental health problems present in metropolitan development and planning. State and local authorities have urged the Service to provide more adequate guidance on these problems. The National Advisory Health Council, the American Public Health Association, the Association of State and Territorial Health Officers, and the White House Conference on Children and Youth, all have recommended that an urban environmental health planning and development activity be developed and supported.

HEALTH ASPECTS OF METROPOLITAN PLANNING

We have started a program on environmental health aspects of metropolitan planning and development, as a new and vital activity to meet the need. Through it, technical and administrative approaches can be developed on troublesome urban hygiene problems. Already some tangible results have become available in terms of a community environmental health planning guide which has been used in several metropolitan areas. Technical assistance and consultation has already been provided to several additional communities. This approach identifies and shows how specific health needs can be met by community capabilities. We propose to expand this phase of the activity immediately.

One activity of the Service to improve urban environment concerns the disposal of refuse and solid wastes. Recently the American Public Works Association, by resolution, requested the Public Health Service to strengthen and expand its current studies on solid wastes disposal methods. There are glaring inadequacies in solid waste collection and disposal practices in the majority of our cities, yet $2 billion is being spent annually for these services.

Refuse collection and disposal techniques have remained fundamentally unchanged over the past half century except for some changes in collection equipment. Refuse disposal facilities have been found to be inadequate in 90 percent of the 9,000 communities with populations of over 1,000. Here, a small amount of national assistance and leadership in the development and application of better and more effective techniques would be helpful in finding solutions to the health and economic problems involved. We propose to start some studies from which to formulate needed criteria, standards, and improved techniques for solid waste programs at the local level.

Our program also includes a wide range of technical assistance on such other community and rural sanitation problems as residential and institutional water supply and sewage disposal, swimming pools, plumbing, parks and recreational facilities, and trailer courts.

We are currently reviewing and evaluating in considerable depth, the activities of the Public Health Service in these program areas. Our studies to date show clearly the need to focus more emphasis on the many problems which are plaguing local urban and metropolitan agencies, and our request reflects this viewpoint.

RESEARCH GRANTS AND TRAINING

The request also provides funds for a research grant program related to these specific program areas, and for specialized training of professional personnel from State and local agencies to help them cope with problems arising from changing technology.

For fiscal year 1962, the request for these activities is $5,604,000. This is an increase of $1,056,900 over the 1961 level. Of this increase, the major portion, $762,000, is for research grants, $63,900 to expand our training activities, and $231,000 for interstate milk, food, and community sanitation activities.

Mr. Chairman, I shall be glad to answer any questions you may have concerning these environmental engineering and community sanitation activities.

BUDGET REQUEST FOR 1962

Mr. Fogarty. What did you ask the Bureau of the Budget for? What was your original request?

Mr. Gilbertson. Our original request, Mr. Chairman, was $6,214,000.

Mr. Fogarty. And you got what?

Mr. Gilbertson. The request is $5,604,000 now.

Mr. Fogarty. You were only cut $600,000. They treated you a little bit better than the others.

INSPECTION OF INTERSTATE CARRIERS

If you have been putting any increased work in on the railroad dining cars and airlines, I have not noticed it in the trains and airplanes that I ride in.

Mr. Gilbertson. Mr. Chairman, during this past year——

Mr. Fogarty. I think they are getting worse and worse.

Mr. Gilbertson. We have been able to strengthen the field staff. This is a process of bringing up a large number of carriers with a somewhat limited staff. As you know, there are something like 1,000 dining cars in operation and there are about 2,200 vessels. There are a good many more aircraft. I do not happen to have the figure handy here. Also, the catering points that supply these facilities, of course, come in it, too. We are operating at the present time with something in the neighborhood of about 40 to 45 people in the field, exclusive of clerical.

Mr. Fogarty. And you cannot do much with that, can you?

Mr. Gilbertson. No, sir.

Mr. Fogarty. Some of these sandwiches they serve you on some of the airplanes taste like they have been made up for a week. Have you had that experience yourself?

Mr. Gilbertson. Yes, sir; I have.

1961 APPROPRIATION IN EXCESS OF BUDGET

Mr. Fogarty. Last year the committee provided $290,000 more than you requested. How is that increase being used?

Mr. Gilbertson. Well, during the current year the major emphasis in the use of these funds is for research purposes. You will recall the very urgent needs which were described with reference to research on milk, food, and shellfish problems, as well as some of those related to the carrier activities. We have initiated studies primarily at the Sanitary Engineering Center in Cincinnati and research on such problems as how pathogenic organisms develop toxins; food services and its relationship to the current public health practices that are used in the field. As a matter of fact, some of the research undoubtedly will find its way into application before very long, because of the work we are doing on revisions of the Public Health restaurant code and ordinance. The industry is working with us on this, and despite the fact that lowering the temperature requirements would result in a heavy expenditure by industry, such research does produce convincing evidence that this needs to be done. These are the only ways we see of actually controlling these food-borne outbreaks.

SHELLFISH

Mr. Fogarty. You mention in your prepared statement that you have found paralytic poisons in shellfish.

Mr. Gilbertson. Yes, sir.

Mr. Fogarty. What kind of shellfish?

Mr. Gilbertson. Mussels and clams on both coasts.

Mr. Fogarty. What do you mean by "paralytic"?

Mr. Gilbertson. Paralytic poison is an unusually toxic substance for which there is no known antidote that is found in certain shellfish, particularly in the waters along the Maritime Province of Canada and the New England coast, and on the northwest coast and on up around Alaska. This toxin appears to be associated with a microorganism, small plant life that grows in the water, and through some process which we do not fully understand, this paralytic poison is formed. When this happens, of course, the shellfish are extremely dangerous to eat. There have been a number of deaths due to eating such mussels and clams, and our work has been concentrated on two phases of the problem.

First, work to make it possible for ourselves and for the State authorities to have a rapid detection method so that we can determine when this condition occurs, before it gets too late; and, second, to learn more about the environment that results in the production of this toxin so that the predictions can be made earlier. This would be of immense help not only to the authorities in the States who have to watch and patrol these waters, but also in connection with industry operations.

It is a very dramatic type of problem. It is, as I said, one of the most toxic of substances, and there is no antidote for it.

Mr. FOGARTY. It has been said that this hepatitis outbreak in Mississippi was traced to polluted oysters.

Mr. GILBERTSON. Yes, sir. We had a very serious outbreak during the past 2 or 3 months actually, which was traced to raw oysters that were harvested from the Pascagoula, Miss., area. This outbreak, on which the Communicable Disease Center of the Public Health Service was called in, along about the first day or two of February, indicated that there was a common food source here, and it looked like raw oysters were at the root of the problem. The Communicable Disease Center got in touch with us and we have some people who were experienced in shellfish operations, and got them into it the next day. It was shown that oysters had been harvested in an area which was polluted. As we looked into the matter further we found that some of these shellfish had been shipped into other areas besides the immediate locality. Some of them were shipped to Mobile, and some of them to Troy, Ala. In all there were about some 100 cases in the three foci and, as you know, the incidence of infectious hepatitis is high this year. Some 60 of these cases appeared to be, on the basis of epidemiological evidence, associated directly with the eating of raw oysters.

We also found some shipments had been made to other localities, and we got in touch with the health authorities in these other localities. We also informed all of the State health officers of the specific shippers involved, and gave them the code number or certificate number that these shipments carried, so that they could take steps to remove any contaminated shellfish from commercial channels, which might be in those channels. We found, in working with the Mississippi State health authorities on the outbreak that some additional studies of the growing waters in that area were needed. We found these waters to be contaminated and, as a result, recommended to the State, which recommendation they followed, that the shellfish growing area be closed all the way from Pascagoula westward over to Biloxi, which is about a third of the Mississippi growing water area.

This has pointed up to us some very serious problems in the whole shellfish program. We have been concerned for a number of years about the growing amount of population and industry on coastal waters, and its effect with regard to the pollution of waters, and the effect on shellfish. During the past year we have initiated some preliminary studies with reference to what additional research was needed. As a matter of fact, in 1959 we had a shellfish research conference which pointed up some of these problems. This conference consisted of a group of experts in this field, from various States, and other Federal agencies, universities, and the industry. You may recall, Mr. Chairman, that several years ago we had a laboratory up in the New England area. Later, this laboratory was moved to the gulf coast, and since we were receiving a large number of requests for assistance on the west coast we recently moved it out there. So it has been in three different locations. Unfortunately, the problems we were working on in the other two areas continued to go on.

SHELLFISH SANITATION RESEARCH CENTERS

Mr. FOGARTY. The Oyster Institute has written to you, haven't they, requesting that more laboratories be set up because of this problem?

Mr. GILBERTSON. The industry association has discussed with us the problems that they see, and we are giving very definite consideration to the problems they raised which fall into four general classes. These are the known ability of shellfish to concentrate materials, not only bacteria, but also certain chemicals and toxic agents, and radioactive materials. We do not really know too much about what they do with viruses, except that we have had this one very serious experience.

Mr. FOGARTY. Please supply for the record a statement relative to the need for research centers and what could be done if you had the funds.

(The statement requested follows:)

STATEMENT RELATIVE TO THE NEED FOR ADDITIONAL PHS SHELLFISH SANITATION RESEARCH CENTERS

I. *Introduction.*—The PHS has, for many years, participated with the States, in a cooperative program designed to insure that fresh or frozen oysters, clams, or mussels shipped in interstate commerce will be safe to eat. This cooperative program has been found necessary because of the peculiar ability of these species to concentrate pathogenic micro-organisms, chemicals, radioactive materials, and powerful marine toxins from their aquatic environment. In support of these control programs, which are carried on by State health or conservation agencies, the Public Health Service has maintained a shellfish sanitation research program at a small laboratory which, since its establishment in 1948, has been successively located at Woods Hole, Mass.; Pensacola, Fla.; and, currently at Purdy, Wash. The work has been confined to investigations of the rate at which shellfish accumulate bacteria and the influence of commercial practices on the quality of the finished product as marketed. Some investigations on paralytic shellfish poison have also been carried on at the Robert A. Taft Sanitary Engineering Center at Cincinnati, Ohio.

The PHS and the States have been seriously concerned by the inadequacy of the research program. The small size of the facility and its present location on the west coast has limited the amount and quality of the specialized technical services which can be provided to States on unusual sanitation problems, has prevented the PHS from completely fulfilling its responsibilities for evaluating procedures used by State laboratories, and has made it impossible to undertake investigations of new public health problems of concern to the shellfish industry. Particularly, the present scope and location of the research is deficient with respect to problems confronting the east coast and gulf coast areas. This latter inadequacy was demonstrated by the recent outbreak of infectious hepatitis attributed to the consumption of raw oysters harvested from a sewage polluted area on the gulf coast. A similar outbreak occurred in Sweden in December 1955, and therefore, there was a warning that fundamental information was needed on the survival of the virus in sea water, and of its ability to survive and perhaps multiply in living shellfish.

A similar situation prevails with respect to the accumulation of chemicals and radioactive materials by shellfish. For example, the Japanese have reported 83 cases of mercury poisoning due to the consumption of fish and shellfish which had accumulated lethal quantities of organic mercury discharged by a plastic manufacturing plant. Similar plants are, of course, operating in the United States and in at least one instance a similar waste is discharged to a river which eventually flows into oyster producing areas.

II. *Needs.*—In the past the United States has been fortunate in having relatively large estuarine areas remote from sources of pollution. However, this situation has changed rapidly as the result of our population increase and increasing industrialization along the coasts.

As a consequence of these combined pressures, areas formerly beyond any suspicion of pollution must now be carefully evaluated. Despite the construction of sewage treatment plants, which cannot completely eliminate pollution, there is an increasing number of areas from which the harvesting of shellfish for direct marketing must be questioned. In these latter cases, it will be necessary that methods be adopted for shellfish purification just as water treatment plants purify water before it is pumped into the distribution mains. Industrial progress has also posed a host of chemical pollution problems unknown only a few years ago. The ability of shellfish to concentrate chemicals, including insecticides, from their environment makes it imperative that reliable information be obtained on chemical assay procedures, on the rates at which shellfish accumulate various chemicals, and on the mechanisms which regulate such accumulation. The occasional presence of paralytic shellfish poison in commercial species of shellfish has been known for centuries; however, it is only recently that reliable assay methods and an understanding of ecology of the toxin has reached a point which makes it possible to provide reliable public health protection without economic loss to the industry. The ability of shellfish to accumulate radioactive materials poses another vexing problem. The rapid increase in the use of nuclear power and the correlative discharge of wastes from nuclear-fuel manufacture and reprocessing dictate a need for research on the problem of accumulation and retention of radioactive material by shellfish.

Shellfish sanitation research is further necessitated by the geographic dispersion of the production areas; the fact that different shellfish species are found in each of the four major growing areas; species characteristics which influence the accumulation and retention of the various polluting materials; and constantly changing commercial practices.

It is important to note that the need for laboratory facilities is not entirely defined in terms of purely research needs. PHS responsibilities in the cooperative program for the certification of interstate shellfish shippers require that the Service assist the States in translating research findings into programs which will provide effective public-health protection for shellfish consumers. This obligation requires that laboratories take an active part in PHS appraisals of State shellfish sanitation programs, in assisting States with the investigation of unusual technical problems, and in training State personnel in the use of new techniques.

III. *Proposed establishment of additional Public Health Service research facilities.*—A review of the current shellfish research situation indicates that additional research needs are most urgent in the New England-North Atlantic and gulf coast areas. This, coupled with the need for providing technical services to the State shellfish program in the geographic region being served, suggests that such laboratories would be most effective if established in the Mobile Bay, Ala., and Narragansett Bay, R.I., areas.

These laboratories should be equipped and staffed to undertake research in each of the four major technical areas—microbiological, marine toxin, chemical, and radiological. The laboratories should, however, be so oriented that they would, in addition to undertaking both basic and applied research, also provide expert staff assistance in PHS review of State programs, technical assistance to States on problems of unusual nature or importance, and specialized training (short, topical courses, and refresher courses) for State and Federal shellfish sanitation specialists and laboratory workers. The laboratories would thus function as regional shellfish sanitation centers.

The establishment of these two additional research centers on the northeast and gulf coasts and the retention of the present west coast laboratory would meet the most pressing program needs; however, it is recognized that the Chesapeake Bay area also has an important shellfish industry and that Alaska has a large, but unrealized potential for the production of clams. It may eventually prove desirable to consider laboratory facilities in each of these areas.

IV. *Summary.*—Increasing population and industrialization have greatly complicated the technical problem of assuring a supply of shellfish which are safe to eat. To meet these needs additional PHS shellfish sanitation research centers should be established immediately in the Mobile Bay (Ala.) and Narragansett Bay (R.I.) areas. The need for such facilities has been discussed with the States involved and initial steps have been taken to plan the facilities needed.

USE OF INCREASED FUNDS REQUESTED FOR 1962

Mr. FOGARTY. You have a $762,000 increase for research grants. Is that right?

Mr. GILBERTSON. Yes, sir.

Mr. FOGARTY. Will you supply for the record, in general, the type of research that this is and to whom are the grants made?

Mr. GILBERTSON. Yes, sir.

Mr. FOGARTY. And also the rest of your increase of $294,000 for direct operations. Put in the record how you plan to use this increase, and why it is necessary.

(The information required follows:)

RESEARCH GRANTS

Areas of research include: food microbiology, the etiology, epidemiology, and pathology of foodborne disease; the factors relating to the health and desirability as a food source of animals, fowl, fish, and shellfish: the toxicology or pathogenicity of food, food ingredients, and materials used in food preparation; the effect of environmental factors upon the keeping quality, nutritive value, digestibility, bacterial or viral flora, and the safety of the product; studies of the administration of milk, food, and shellfish sanitation programs; metropolitan engineering and planning; environmental health aspects of man's shelter; interstate carrier; a range of environmental factors such as insects important in food production; and organization and administration of pertinent State environmental health programs.

Breakdown of projects recommended for approval as of Mar. 20, 1961, by subject of research

Subject matter	Number of projects	Amount
Food technology	32	$415,042
Food microbiology	21	276,357
Food toxicology	48	897,070
Milk technology	8	59,741
Milk microbiology	10	101,097
Milk sanitation administration		25,312
Shellfish technology and marine ecology	8	172,621
Insect control and resistance	10	317,190
Solid wastes disposal	3	58,095
Private waste and water treatment	5	78,388
Environmental physiology	3	54,030
Institutional environmental microbiology	2	110,673
Subtotal	150	2,565,616
Anticipated recommended approvals before close of fiscal year 1961	16	246,000
Total	166	2,811,616
1961 budget		2,548,000
Anticipated backlog at close of fiscal year 1961		263,616

Breakdown of projects recommended for approval for funding as of Mar. 20, 1961, by type of institution and department of grantee

Type of institution and department	Number of projects	Amount
University:		
Engineering	8	$123,572
Milk and food technology	58	931,273
Physical sciences	12	171,485
Biological sciences	41	563,766
Biomedical sciences	15	246,167
Public health	3	56,626
Subtotal	137	2 092,889
Public health agencies	3	227,591
Other public agencies	3	81,722
Private research institutions	7	163,414
Total	150	2,565,616

The increase will permit the awarding of the same amount of new grant projects in 1962 as were awarded in 1961. These include studies on the identification and significance of chemical residues in food, and tidewater ecology in relation to shellfish sanitation and safety, and administration of State environmental health programs.

INCREASE IN DIRECT OPERATIONS

The increase of $294,900 for the "Milk, food, interstate, and community sanitation activity" in 1962 provides additional support in the following program areas:

Activity	Program increase	Annualization of new positions in fiscal year 1961	Total
Milk sanitation	$38,000	$31,700	$69,700
Shellfish sanitation		13,400	13,400
Food-service sanitation	23,300	12,600	35,900
Interstate carrier	30,000	17,040	47,040
General engineering		7,060	7,060
Metropolitan planning	26,000		26,000
Solid wastes engineering	9,000		9,000
Training	63,900		63,900
Research grants, review and approval	10,000		10,000
Bureau of State Services management fund	2,900		2,900
National Institutes of Health management fund	10,000		10,000
Total	213,100	81,800	294,900

MILK SANITATION

With the program increase of $38,000, we will have four positions (two professional and two aids) to start urgent work on evaluating bacterial standards in the light of changing processes in the fluid milk industry. As a result of technological developments, new technical procedures and administrative practices must be developed and tested to maintain satisfactory health protection.

FOOD-SERVICE SANITATION

Food infections and food poisoning continue to be an important cause of communicable disease. Field trials and demonstrations of the sanitary provisions of the new food-service sanitation manual will be conducted in three different locations. In order to conduct this project on an effective basis, it will be necessary to carry it out through the established field offices of the Public Health Service (eight regional offices). With the $23,300 increase (three positions) it will be possible to begin work in three areas.

INTERSTATE CARRIER SANITATION

The increase of $30,000 is needed to investigate the relationships between quality of water supplies and certain diseases. Findings of the study will be used in the development and application of drinking water standards used by the Service in certifying public water supplies for interstate carriers. The health benefits of the interstate carrier sanitation program, of course, extend substantially beyond the 2 million daily passengers on interstate public conveyances.

METROPOLITAN PLANNING; ENVIRONMENTAL PROBLEMS

An increase of $26,000 is provided to strengthen immediately our activity on metropolitan planning and development. There is a pressing need to incorporate health considerations and health competencies in solving urban problems. Several major national organizations have adopted recommendations urging the Public Health Service to expand its program as a vital part of the national effort. Two examples are as follows:

Association of State and Territorial Health Officers recommends: "That State health departments initiate and participate in metropolitan health planning to facilitate cooperation among health, planning, public works, and public welfare agencies in meeting the present and future needs of expanding communities; and that the Public Health Service be requested to conduct training, research, and field studies in this area."

National Advisory Health Council recommends: "The Public Health Service should strengthen substantially activities for aiding State and local programs which are needed to deal with problems of metropolitanism. Broad and basic studies on political, social, and economic, as well as technical aspects of environmental health should be initiated. Provision should be made for conducting and supporting research and investigations, technical assistance, training, and demonstrations in the environmental health aspects of metropolitan planning, community development, and housing hygiene."

The increase will provide for four positions for field activities to assist State and local agencies.

SOLID WASTES ENGINEERING

Technical assistance will be provided State and local health agencies on current problems in the disposal of refuse and solid wastes. This is one of the most neglected of environmental problems. Yet over $2 billion is expended annually in the United States for refuse collection and disposal operations. Practical studies to improve solid wastes programs at the local level will be initiated. Nine thousand dollars for the support of one position on this project is requested.

TRAINING

There is an urgent need for expanding technical training to equip professional personnel of Federal, State, and local agencies with the knowledge and skills required to cope with new technology. The proposed increase of $63,900 will permit three new courses at the Sanitary Engineering Center, and three new field courses, in presently neglected fields. An additional 144 persons will be trained.

ENFORCEMENT POWERS

Mr. Fogarty. What are your enforcement powers in connection with interstate and community sanitation?

Mr. Gilbertson. Mr. Chairman, these are primarily related to the authority that the Service has to control the interstate spread of communicable disease. Under this broad power certain regulations have been issued which include the shipment of certain infectious materials. They include the traveling of people who are known to be infected; and, in the sanitation department, the conveyances, including buses, aircraft, vessels, and trains.

Mr. Fogarty. If you find something that is very unsanitary, can you seize it, as the Food and Drug Administration can?

Mr. GILBERTSON. On food we do not have a specific seizure power unless we can show that right then and there, I believe, it would be causing the transmission of disease. I might mention in addition the other type of programs which we carry out, which relate to interstate shipments, that is, the interstate shipment of milk, and the interstate shipment of shellfish. These are carried out under the broad authority to assist States, and the programs are voluntary ones in which the States exercise the control and carry out the inspection, and carry out the actual control operations.

The responsibility of the Public Health Service under these agreements is to carry out an overall surveillance, checking and evaluating these State programs. It was in this connection, I think you will recall, that we received some criticism 2 years ago because the Service was not carrying out its end of the bargain. We have attempted to strengthen these areas during the past year.

DIFFERENCE BETWEEN PHS AND FOOD AND DRUG ACTIVITIES

Mr. FOGARTY. How does your work differ from that of the Food and Drug Administration?

Mr. GILBERTSON. The Food and Drug Administration is responsible for administering the Food, Drug and Cosmetic Act, which has in it the establishment of what are entitled "standards of identity" for foods. In other words, this defines what the product is and what it shall consist of. FDA also carries out certain laboratory objective examinations on foods shipped interstate.

On the other hand, the Public Health Service's work is primarily designed to assist State and local agencies, particularly on problems which are not interstate, and there are many of them. In fact, expressed in total volume, the major portion of foods do not go interstate in their shipment. So we use our facilities to carry out research, and we use our field activities to back up the State and local agencies. The two exceptions from that are the ones I mentioned earlier of the interstate milk and shellfish certification programs. In these cases we have a working understanding with the Food and Drug Administration.

PLUMBING STANDARDS

Mr. FOGARTY. Are you familiar with the letter that has been written to this committee by the National Association of Plumbing Contractors?

Mr. GILBERTSON. No, sir, I am not.

Dr. ANDERSON. Yes. That is the one that Mr. Michel gave to us.

Mr. FOGARTY. They say that a comprehensive program of research on standards for plumbing by the U.S. Public Health Service is urgently needed to permit their industry to keep pace with other phases of the building industry, and to provide the greatest benefit to the public. Have you given any thought to that?

Mr. GILBERTSON. Yes, sir. We have given the overall problem of the public health aspects of plumbing a good deal of thought. I believe you will recall several years ago this matter did come up before this committee, and at that time we reported to you that we were carrying out some staff assistance in connection with the development of plumbing standards. It is staff assistance to a technical committee which is operating in this area.

Mr. Fogarty. It was a little controversial, was it not?

Mr. Gilbertson. Yes, sir. That is right. There was some opposition, and I believe there was some support. In fact, it was quite surprising that this level of activity would generate that much interest, because I believe we reported to you at that time that we were spending about $5,000 a year on it. We have continued at about this same level.

Mr. Fogarty. I think that is all for today. We will come back at 10 o'clock tomorrow morning.

Tuesday, March 21, 1961

POSITION OF CONFERENCE OF SANITARY ENGINEERS ON SHELLFISH PROGRAM

Mr. Fogarty. The committee will come to order. When I went back to my office last night I received this letter from the Conference of State Sanitary Engineers. It is their statement of position in regard to the shellfish sanitation program. Do you know anything about it?

Mr. Gilbertson. Yes, sir.

Mr. Fogarty. What do you think of it?

Mr. Gilbertson. We understand that they are equally concerned with us in the problem of laboratory backup for the shellfish programs. Due to the recent outbreak of infectious hepatitis, this problem has come to the fore again very strongly.

Mr. Fogarty. I am going to put it in the record now. You may expand on your remarks concerning it.

(The letter referred to follows:)

Conference of State Sanitary Engineers,
State Board of Health,
Topeka, Kans., March 17, 1961.

Hon. John E. Fogarty,
House of Representatives,
Washington, D.C.

Dear Mr. Fogarty: The attached statement of position was adopted on March 17, 1961, by the executive board of the Conference of State Sanitary Engineers during its current annual meeting. It relates to a definite need, as we see it, for the Public Health Service to expand its activities in the research and field study aspects of its shellfish sanitation program.

The recent outbreaks of infectious hepatitis in Mississippi and Alabama, which have been attributed to the consumption of raw oysters from polluted waters, point up the need for continuous investigations of shellfish sanitation problems in each of our major shellfish producing areas and for the resources necessary to assist States in the investigation of specific problems which may exceed the capacities of individual State facilities.

Any assistance that you may be able to provide in bringing about the establishment of such additional shellfish research facilities by the Public Health Service will be appreciated.

Sincerely yours,

Dwight F. Metzler, *Chairman.*

Statement of Position of Executive Board, Conference of State Sanitary Engineers, Relative to Public Health Service Shellfish Sanitation Research

The Public Health Service and the States have for many years cooperated in a program designed to insure that fresh or frozen shellfish shipped in interstate commerce would be safe to eat. This program was instituted in 1925 following a large typhoid epidemic which had been attributed to oysters—one of many such outbreaks in which bivalve shellfish had then been implicated. As a part of its responsibilities under this cooperative control program, the Public Health Service has carried on a series of studies on shellfish bacteriology. The laboratory at which these studies have been centered has been successively located at Fisherman's Island, Va., Craney Island, Va., Woods Hole, Mass., Pensacola, Fla., and Purdy, Wash.

The executive board, CSSE, recognizes that this PHS laboratory has made substantial progress in the investigation of shellfish bacteriology in the several areas in which it has been located. However, the frequent relocations of the laboratory, necessary to meet most pressing needs, has severely limited its effectiveness and, in many cases, has prevented the maximum utilization of the technical information developed by the PHS laboratory and by the State laboratories that have collaborated in these investigations. The executive board wishes to point out that (1) there is a need for continuing research on the bacteriology of shellfish, and (2) that the research needs of the four major shellfish-producing areas are not identical because of fundamental differences in hydrography, climate, and species of shellfish, and (3) that States must frequently seek technical assistance from PHS in meeting unusual shellfish sanitation problems. It is accordingly recommended that the Public Health Service expand its research in shellfish sanitation through establishment of regional shellfish sanitation laboratories.

Future research at the Public Health Service shellfish sanitation laboratories should not be limited solely to the investigation of bacteriological problems. Thus, in some areas the control of paralytic shellfish poisoning is an important component of the State shellfish control program. In such areas it would be important that the laboratory be equipped for continuing investigations of this problem. The recent outbreak of infectious hepatitis associated with oysters also demonstrates that health authorities must now be concerned with the presence of pathogenic viruses in estaurine areas. Adequate public-health control of this problem will ultimately require much additional research on the survival of viruses in sea water, the accumulation of viruses by shellfish, and the survival, or possible multiplication, of viruses within the living shellfish. The ability of shellfish to concentrate insecticides or other chemicals, and radioactive materials from the aquatic environment strongly indicates that these PHS regional shellfish sanitation laboratories also have facilities and staff which would enable them to carry on necessary research in these fields.

The executive board recommends that the Public Health Service give consideration to the needs for laboratories to conduct research in the bacteriological, chemical, radiological, and virological aspects of shellfish sanitation and that plans be made for establishing laboratories on the west coast, the gulf coast, and the east coast.

EXPANSION OF MR. GILBERTSON'S STATEMENT ON NEED FOR STRENGTHENING SHELLFISH SANITATION RESEARCH

The need for immediate establishment of Public Health Service shellfish sanitation laboratories on the gulf and northeast U.S. coasts has been discussed in detail in the statement submitted to the committee in accordance with the chairman's previous request. As indicated in that statement, we believe that these research and technical program backup needs would be best met through the establishment of new PHS facilities in the Mobile and Narragansett Bay areas. We also believe that we should expand our facilities at the existing Purdy, Wash., shellfish sanitation laboratory to permit us to conduct studies on accumulation of chemicals and radioactive materials by shellfish.

We estimate the cost of constructing and equipping these two field laboratories—which would be of the temporary facility type—at approximately $1,570,000, exclusive of site ($685,000 for each laboratory plus a shellfish purification pilot plant for the northeast-New England coast). Construction can probably be completed within 6 to 9 months. We visualize an employment of professional and subprofessional staff of approximately 50 persons. Recruitment and orientation of the technical personnel would be phased to begin utilization of the facilities when completed. Personnel costs would be about $250,000 for the initial (partial) year of operation.

The PHS has recently received a letter from Mr. William Younger, director, Alabama Department of Conservation, suggesting the establishment of a research laboratory in the Mobile Bay area and offering the assistance of the State in procuring land. We have also received a letter from Dr. J. E. Cannon, director, Rhode Island Department of Health, describing the technical advantages of the establishment of a PHS laboratory in the Narragansett Bay area. Mr. Younger and Dr. Cannon have been advised that we are in agreement with their recommendations and that we hope to obtain necessary support for the establishment of these facilities.

OCCUPATIONAL HEALTH ACTIVITIES

Mr. **FOGARTY**. The next activity is "Occupational health activities." Dr. Magnuson, do you have a statement for the committee?

Dr. **MAGNUSON**. Yes, Mr. Chairman. With your permission, I shall file with the committee the formal statement regarding the activities of the Division of Occupational Health and shall confine my remarks to a few highlights which I believe to be of interest.

Mr. **FOGARTY**. All right.

(The statement follows:)

STATEMENT BY CHIEF, DIVISION OF OCCUPATIONAL HEALTH, ON OCCUPATIONAL HEALTH

Mr. Chairman and members of the committee, it is a privilege to present this report on occupational health which now represents a part of the environmental health activities of the Public Health Service.

Occupational diseases are as old as man's efforts to make a living. Although the character of the environment in which he works has changed radically through the centuries, each innovation has brought its own occupational health hazards.

In contrast to acute, large-scale disasters such as the 476 workers who died from silicosis in 2 years and the 1,500 others who were disabled while constructing the Gauley Bridge tunnel, today's occupational health hazards are less apparent and more insidious and devious in their manifestations. They may be grouped in three classes:

(1) The old problems which doggedly persist, either because known controls are not conscientiously applied, or because additional basic knowledge is needed to reduce further the incidence of disease.

(2) New problems which arise from the multiplicity of untried toxic agents being applied in industry, and from the introduction of new processes.

(3) A gray area of chronic diseases where the occupational relationship is suspected and which will require deeper probing.

Still another significant change affects the course and progress of occupational health. There has been a heightened awareness of the effects of the growing chemical world surrounding us. Many of these problems were discussed before this committee last year and printed in the report on environmental health problems. Although this manmade environment encompasses the whole of our civilization, special attention should be given to the occupational factor. It is in the inplant environment that many of the toxic pollutants now threatening the air and water of communities throughout the Nation are first spawned. The industrial worker is first exposed to the plethora of chemicals that find their way into home use. It should be recognized that industry is the incubator for problems of more far-reaching consequence, and that alert, scientifically sound and completely unbiased investigations of occupational health problems can often prevent illness, or at least provide the basis for later communitywide investigations.

A NEW MULTIPRONGED ATTACK

Last year, on the recommendation of your committee, additional support was given to the occupational health program in order that the Public Health Service might more adequately fulfill its responsibilities and enlarge its research activities, particularly in toxicology.

With its increased appropriation, the Division of Occupational Health has geared itself to meet more effectively the changing character of the occupational health problem. The additional money appropriated in 1961 has made possible a beginning in achieving new direction and depth in research, and in related efforts aimed at protecting the health of American workers.

Intensified field study efforts, for example, are now yielding definitive figures on the health effects of certain occupational exposures. Thus, the expansion of the study in metal mines, being conducted jointly by the U.S. Bureau of Mines and the Division of Occupational Health of the Public Health Service is revealing that silicosis continues to be a problem in an industry where it was believed to be largely vanquished. The initial surveys will have been completed in late 1961, by which time it is anticipated that 15,000 miners and 75 mines will have been examined. The study has now moved out of the Western States and is covering midwestern and eastern mines. This study is opening the door to more fundamental research on such factors as the significance of smaller dust particles, individual susceptibility, and the role of the immunologic response in silicosis.

The study of health hazards associated with uranium mining and milling is also being strengthened. This study has now reached a crucial stage. Deaths are occurring in excessive numbers due to lung cancer and to complications of silicosis. To focus full attention to this problem the Secretary of Health, Education, and Welfare called a conference on December 16, 1960, to meet with represenatives of the Federal Government, the Governors, and other officials of the States concerned with the uranium mining problem. As a result, accelerated efforts are being made to complete definitive examinations on all uranium miners and to spur those who have been dilatory in complying with recommended measures to control environmental hazards in the mines.

TOXICOLOGIC STUDIES

The increased appropriation has permitted also a more vigorous toxicologic program. Major effort has centered on undertaking and expanding work in two basic areas of toxicologic investigation. The first is an evaluation of an immunologic approach to toxicologic responses. Work of Vigliani in Italy and Scheel in our own laboratories, as well as certain of our field studies, has shown that for many chemicals the response is not one of direct chemical injury, but rather a complex process in which immunologic processes analogous to those observed in some of the infectious diseases may be the critical factor. The second area under investigation is a study of enzyme systems. It is realized that damage to cells and to tissues in the body first takes place by interference with certain essential enzyme systems. Work in our own laboratories has shown that such subtle changes in enzyme systems may be detected in certain types of heavy metal poisoning, as well as the result of poisoning from some solvents. Exploitation of this finding and an extension of such observations will permit the early identification of people who should be carefully protected from certain types of work environment, thus forestalling needless and often permanent damage.

Toxicologic studies are being made to determine how certain types of toxic substances found in the industrial atmosphere neutralize one another, while others enhance toxicity; the toxicity of oil mists; how industrial chemicals act on protein films as a mechanism model of lung injury; and changes in biochemical profiles of men and animals occurring as a result of exposure to chemicals.

It has been demonstrated that the inhalation of nonliving toxic agents produces a reaction in the body that may be anything but direct and simple. The inhalation of ozone, for example, at concentrations that end ultimately in edema of the lungs, slows the uptake and release, temporarily, of iodines by the thyroid. The possibility that the nervous system is the triggering mechanism holds great implications for work on the toxic effects of industrial agents.

Further toxicologic research has included the mechanisms of the pulmonary effects of oxidant gases, pharmacologic mechanisms of protection against oxidant toxicity, and immunochemical relationships of industrial allergents.

Another study which promises to have great significance in experimental toxicologic methodology concerns the effects of air ions on laboratory animals. Studies are in progress to show whether electrical properties of the atmosphere can produce alteration in response of animals which inhale various types of substances affecting the respiratory tract. One of the effects which has been reported due to negatively ionized air is a decrease in the number of respiratory infections in the population. Preliminary experimental results show a detectable difference between animals exposed to positive air ions and negative ions. The differences appeared in the lung to body-weight ratios, which in the rat provide a remarkably sensitive indicator of alterations in the lung.

Among numerous other projects, studies to find the means by which carbon disulfide affects the nervous system were continued with experimental animals. It has been found that early metabolic changes caused by overexposure to carbon disulfide are associated with changes in contents of certain metals in various tissues of the body, particularly the nervous system. These metal displacements from the tissues, apparently involving copper and zinc, are detectable before the effects on the nervous system of carbon disulfide become apparent. The theory that changes in tissue metal content may be the critical mechanism involved in carbon disulfide poisoning was supported by the reduction in the time of onset and severity of nervous symptoms in animals which had metal-fortified diets. This finding is of current importance, since signs of overexposure to carbon disulfide are still occuring in American industry.

UNSOLVED PROBLEM AREAS

One of the principal unsolved problem areas in this field involves the physiologic and psychologic measures of toxic effects. At the present time, nearly all of the American standards for maximum allowable concentrations of chemicals in the industrial environment and elsewhere are based on studies measuring the pathological effects of these chemicals in animals. The Soviet Union and some of the other countries in Eastern Europe believe that physiologic and psychologic changes provide a far more sensitive and a safer method of estimating potential damage, and serve as much more reliable indices for the setting of maximum allowable concentrations. In some instances, this has resulted in as much as a twentyfold difference in the Eastern European recommendations as compared to those used in the United States. As a toxicologic tool, these methods require a most careful investigation and evaluation. Should the methods prove valid, they would not only provide tools for the laboratory evaluation of chemical agents, but would also provide more accessible tools for the determination of the effect of human exposure.

Within the existing resource, emphasis is being placed on analytic research, a vital supportive tool in the prevention, diagnosis, and treatment of occupational disease. This research has concentrated on the development of laboratory techniques involving the use of ion exchange resins for the separation of trace quantities of toxic substances from undesired, bulky components of biological samples. Applications of this technique, based upon selective adsorption and elusion processes, have resulted in the development of methods for the determination of fluoride in fresh urine samples, for the separation of submicrogram quantities of beryllium and of mercury from urine ash solutions, and for the removal of submicrogram quantities of lead from biological samples and chemical reagents. The method promises to be ideal for the typical industrial hygiene laboratory because a minimum of equipment and man-hours are required, and procedures are simple as contrasted with the conventional analytic methods.

OCCUPATIONAL MORBIDITY AND MORTALITY STUDIES

Representative of another approach to the identification and control of occupational diseases are our studies of occupational morbidity and mortality. In the absence of national reporting of occupational disease and in the face of frequent complexity of differential diagnosis, exploration of various sources of data on the health experience of various large groups of employed persons holds promise for yielding valuable clues on possible occupational factors.

A special study of interest involves the analysis of approximately 500,000 permanent disability cases by type of disability and occupation. Standardized relative indices will be provided showing variations in the extent of specfied disabilities among occupational groups. In another study, lung cancer data were extracted from tables prepared by the National Office of Vital Statistics which computed rates on the basis of occupational data reported on death certificates during 1950 and occupational data from the 1950 census.

A code has been developed to provide meaningful information regarding the occupational status of persons interviewed in the national health survey.

TRAINING

Training of professional personnel has been augmented in 1961 through the addition of new, short training courses. Special courses are being offered for physicians, nurses, and State and local health department personnel. In the current year additional 1-week courses on noise and lead analysis will supplement the basic industrial hygiene engineering and chemistry courses that have been offered by the Division. Because these courses have been heavily oversubscribed, the number of times that they are presented will also be increased. As a further means of meeting the need for such training, the Division developed and presented jointly with the Industrial Hygiene Foundation a prototype course for industrial hygiene engineers and chemists in industry. The Division will also work more extensively with other such groups and academic institutions to help develop the professional resources to meet the needs of this rapidly growing field.

Other types of educational and informational activities, directed at professional management and labor groups, are also being augmented, to secure more widespread and effective application of occupational health practices. As part of this effort, the Division of Occupational Health is cooperating with the International Occupational Safety and Health Information Center recently established by the International Labor Organization. The Division is serving as the national center responsible for obtaining abstracts of U.S. literature in the occupational health field. The objective is to provide a complete abstracting and reference service for the world literature on occupational health and safety. Through this project, the exchange of occupational health information on an international basis has been markedly improved.

RESEARCH GRANTS

An increased program of research grants is proposed for 1962, to permit more effective utilization and development of the research knowledge and skills in our universities and in other non-Federal laboratories and agencies, public and private. Among program areas in which an increase in requests for grant-supported research can be anticipated are: Occupational skin diseases, agricultural health, the development of biochemical tests for early detection of toxic chemical effects, and basic studies in the physiologic and psychological effects of various working environments. An increase of $474,000 is requested for these grants.

The appropriation requested for 1962, $3,981,000, will permit a continuation of work begun under last year's expanded program, plus an increase of $474,000 for additional research grants and $50,000 for expansion of the uranium miners project.

Mr. Chairman, I shall be glad to answer any questions on this program and the budget.

INCREASE FOR 1961

Dr. MAGNUSON. Last year, following the hearings on environmental health, your committee recommended that the Public Health Service intensify its efforts in occupational health and made available $1 million in new funds for that purpose. While 1 year is too short a time to overcome all of the gaps that were referred to in last year's testimony, it has permitted us to start.

We have been fortunate in our recruiting efforts. The work in toxicology has been strengthened by the addition of qualified scientists and capable supporting personnel for that activity. The efforts of these scientists are demonstrating important new immunologic and enzyme mechanisms that underlie the body's response to foreign chemicals. I believe these findings are significant for three reasons.

In the first place, they point a way to better testing procedures. I believe that these better testing procedures are our only hope of coping with the avalanche of chemicals that come to us through a vigorous chemical technology. In the second place, these newer techniques point the way to sensitive indicators of action that can be applied to man before irreversible and permanent damage occurs. Third, these same techniques point to the way of developing protective measures and means of evaluating the effectiveness of these protective measures in use.

One of our field studies is now approaching a very critical point. This is our study of the uranium miners, which is now in its 10th year. Evidence indicates that, unless we take vigorous measures now to reduce the environmental hazards of these miners, we are going to harvest a mass of premature deaths due to lung cancer and the complications of silicosis. This will not only place severe burdens on the individuals and States involved, but will also jeopardize the mining of this important metal.

We have been able to begin, through both direct efforts and contracts, statistical studies which will enable us to pierce the fog which has surrounded the incidence and prevalence of occupational diseases in this country. We will be in a position to make effective use of data received from the Bureau of Old-Age and Survivors Insurance, the National Office of Vital Statistics, and the National Health Survey.

STATE PROGRAMS

The unsatisfactory condition of occupational health programs in most States will not be solved overnight, but our accelerated training activities have helped to support the cadre of State workers around whom further growth must be built.

The dissemination of technical information has been augmented by our designation as the national center for occupational health information for participation in the international exchange of information through the International Labor Organization.

In response to a frequently expressed need, we have begun the development of educational materials written in the language of, and directed to, the workman who must himself handle dangerous materials.

The amount requested for 1962—$3,981,000—will sustain the activities started in 1961 and will permit an increase of $474,000 for research grants; $50,000 for expansion of the uranium miners' studies, and a net of $105,500 to maintain the program at the 1961 level.

Mr. Chairman, I shall be happy to answer any questions.

INTERNATIONAL EXCHANGE OF PROFESSIONAL INFORMATION

Mr. Fogarty. Doctor, what did you say about the International Labor Organization?

Dr. Magnuson. This is actually an outgrowth of our own responsibility, sir, in the collecting and making available of technical information. About a year or a year-and-a-half to 2 years ago the International Labor Organization set up an international exchange of this information providing for translation of abstracts into about half a dozen working languages. There are three groups in the United States participating on the United States side: The Division of Occupational Health for occupational health information; the Bureau of Labor Standards of the Department of Labor for occupational safety information; and recently, one of the voluntary agencies in the safety field has also agreed to participate from the United States.

Mr. Fogarty. What agency is that?

Dr. Magnuson. The voluntary agency? I will have to check that, sir. Originally they approched the National Safety Council, but there was a shift. May I supply that for the record?

Mr. Fogarty. Yes.

(Note.—Dr. Magnuson later indicated that the American Society of Safety Engineers is participating in the ILO Information Exchange.)

Mr. Fogarty. How long has this been going on?

Dr. Magnuson. It has been going on approximately 2 years now.

Mr. Fogarty. What benefits have been derived from this sort of a program?

Dr. Magnuson. I believe the benefits are many, because it is bringing together into one place an easily available file of not only the scientific accomplishments in all of the various countries, but also very brief abstracts of legislative changes, regulatory changes, and so on, applicable to the field of occupational health and safety.

It makes available to us very quickly, for example, the information from the Italians, the French, the Germans, the Russians, and so on.

HELPFUL INFORMATION FROM OTHER COUNTRIES

Mr. Fogarty. Has any of the information that has been gathered in other countries been of any help to you in this country?

Dr. Magnuson. It has certainly given us some very definite ideas on things that we would like to be hitting harder in this country.

Mr. Fogarty. What, for instance?

Dr. Magnuson. For example, there are some techniques in the testing of chemicals that the Russians and some of the countries back of the Iron Curtain have been prosecuting very vigorously. One is the so-called performance testing which the Russians developed out of some of their Pavlovian theories.

In brief it amounts to this. Animals that have conditioned reflexes through training are used as the test subjects for exposure to various chemicals. By measuring the changes in these reflexes, these scientists maintain that they have a far more sensitive indicator of what is happening than that provided by the conventional kind of toxicology methods.

For example, in the case of trichlorethylene, which is a solvent used in certain kinds of cleaning operations, the Russians say that our maximum allowable concentration is on the order of 20 times too high. It is a technique that is not very widely used in this country, and one that certainly should be promptly used.

USE OF FUNDS APPROPRIATED FOR 1961

Mr. Fogarty. You are requesting an increase of $629,000 this year. Last year we gave you an increase of over $1 million, considerably more than you requested. What are you doing with that money?

Dr. Magnuson. More than 50 percent of the money that was made available to us last year has been going into the employment of staff, the getting underway of work in toxicology, which I referred to very, very briefly. The toxicology work is headed by our Dr. Stockinger who is one of the outstanding toxicologists in the United States.

In addition to the enzyme studies and the immunologic studies to which I referred, our toxicologists have been doing some very important work developing additional testing methods through the use of lung models. I don't want to mislead you by this, but they have found that by using isolated films of fluid from the lungs and exposing this fluid to various chemicals, they can duplicate very quickly the kinds of injuries they observe in the lungs of animals that are exposed to these same chemicals.

They have run into some very, very interesting kinds of antagonisms with some of these compounds—taking two compounds that are themselves apparently highly toxic, and under certain conditions putting them together and finding that their action tends to neutralize one another. They are doing some highly promising work on the effects of air ions, in which the ions in the air are charged positively or negatively, and finding that these air ions change the toxicity of these various chemicals.

Mr. Fogarty. Could you, in your explanation to a layman, talk more about how it affects human beings' lungs rather than using these technical terms?

Dr. Magnuson. I will try to do that. Our problem is this, sir. If a new chemical is made and comes into being——

Mr. Fogarty. There are hundreds of them being made, aren't there?

Dr. Magnuson. As nearly as we can tell, sir, the organic chemists make somewhere on the order of 5,000 to 10,000. Some estimates are even as high as 50,000, a year. As nearly as we can tell, about 500 of these actually enter into commerce.

Mr. Fogarty. There is no reason to believe that that amount is going to go down next year, is there?

Dr. Magnuson. No, sir.

Mr. Fogarty. It will go up.

Dr. Magnuson. There has been a continual steady growth in this technology. The difficulty that all of us face in this kind of a situation is this. Here is this new chemical. What is it going to do to you and to me? Obviously, we can't run out and get human volunteers and expose them to these chemicals. So at this point we have to rely on various kinds of animal testing.

The best experts in the field tell me that even for the most preliminary kind of toxicologic testing in these animals they have to spend about $100,000 per single chemical tested. Even this doesn't tell the whole story. So here is problem No. 1: What is the better method of testing in this initial stage?

After performing these kinds of tests and developing what seems to be safe kinds of levels for you and me and every person who is exposed to these chemicals, we must await the final proof which depends upon what happens to man over a long period of time. This is tough; it is difficult to determine. Up to this point, by and large, we have been recognizing as occupational diseases those that meet one of two criteria. One is the development of disease so close to exposure that there is no question of the relationship. For example, you were painting with this material and the next day you became sick. The other type of situation is when a particular kind of disease occurs only in a certain kind of occupation and no place else.

SILICOSIS

For example, silicosis develops in people who have been exposed to some form of silica. In those situations there is no question that it is occupational.

Mr. FOGARTY. It took quite a while to make it occupational, though; didn't it?

Dr. MAGNUSON. Yes, sir.

Mr. FOGARTY. I remember some of the unions talking about it years ago.

Dr. MAGNUSON. Our last bad—really bad—episode that precipitated much research work in this country occurred about 1932, in the building of the Gauley Bridge tunnel, which was a hydroelectric tunnel.

Mr. FOGARTY. Supply that story for the record as an example.

Dr. MAGNUSON. Yes, sir.

(The material requested follows:)

About 2,000 workers were engaged in digging a 3-mile rock tunnel for diverting water to a hydroelectric plant at Gauley Bridge, W. Va., during 1932–34. The course of the boring was through hard rock, containing dangerously high amounts of silica. None of the now common precautions in mining practice were observed to protect the men against silicosis. As a result, in 2 years' time, 476 workers died from silicosis and 1,500 others were disabled.

This tragedy was the subject of congressional hearings in 1936 (U.S. Congress, House Committee on Labor Subcommittee: "An investigation relating to health conditions of workers employed in the construction and maintenance of public utilities," H.J. Res. 449, 74th Cong., Washington, D.C., U.S. Government Printing Office, 1936).

There also followed an intensification of the Public Health Service's research efforts, and during the period 1934–40 five major investigations were conducted on health hazards in the dusty trades. In the midthirties, funds made available under the Social Security Act also enabled the Service to stimulate the establishment of occupational health units in State agencies to help apply the findings from these and other occupational disease studies.

Mr. FOGARTY. Go ahead.

Dr. MAGNUSON. Following this work, following the Gauley Bridge incident, there was quite a bit of work done by the Public Health Service to develop safe working standards for this kind of operation. A great deal of work was done at that time by the Division of Industrial Hygiene to develop such standards prior to World War II.

There is no question that these standards are adequate to prevent the development of the acute kind of episode that we saw in the Gauley Bridge disaster, where these men died within a matter of a couple of years. Now, instead of acute kinds of disasters, we are seeing silicosis develop 15 or 20 years later in men who have been working in the mines. We haven't eliminated the disease; we have merely reduced the incidence.

So this is one of the things which we are investigating with our silicosis surveys of the mines, which we have been carrying on for over a year and a half now.

Mr. FOGARTY. A group came before us 2 or 3 years ago and wanted us to do something about this and there was extra money put in the bill.

RESEARCH GRANTS

Four hundred and seventy-four thousand dollars of the increase is for research grants. What type of research is this and where is it being done?

Dr. MAGNUSON. This is research in which the kind of work that the man does is the critical variable.

Mr. FOGARTY. Give us a couple of examples.

SILO FILLERS' DISEASE

Dr. Magnuson. For example, one of the important research projects that is going on is being carried on in one of the Middle Western States, involving a disease known as silo fillers' disease. What happens is that in the fermentation process by which silage is formed, significant quantities of one of the oxides of nitrogen are formed. This is a rather toxic chemical.

If a farmer is exposed to this chemical, he develops either an acute or chronic lung condition. In the studies being carried out by this midwestern group, it has been found that about 4 out of 5 of the silos surveyed have had levels of nitrogen oxide that are in excess of what they feel are safe concentrations.

They have, in addition, worked out ways in which certain reducing materials can be added to this silage to prevent the oxides of nitrogen from forming.

Mr. Fogarty. How would these gases affect a man?

Dr. Magnuson. They will affect him in one or two ways. He can become acutely ill and even die if the concentration of the gas is sufficiently high.

If the man doesn't die, if the concentration isn't that high, he winds up as a lung cripple, if you will. The gas has irritated the lung passages and there are various degrees of tissue changes. So the man just does not have the lung capacity he should have.

Mr. Fogarty. Give us another example.

OCCUPATIONAL FACTORS IN CAUSE OF DEATH

Dr. Magnuson. One of the other important kinds of work that we are supporting is a project at the University of Pittsburgh to study the effects of kinds of occupation, economic level, and so on on the ultimate cause of death of a wide segment of workers in this country. This is possible through the proper use of the kind of data made available through the Bureau of Old-Age and Survivors Insurance.

Once a man has died, you can check back as to what he had been working on and compare that against the various causes of death. It is the kind of information that is badly needed in this country, and I am delighted the University of Pittsburgh is undertaking this project.

There are a number of other projects related to——

Mr. Fogarty. You can supply a few more for the record.

Dr. Magnuson. Yes, sir.

(The information requested follows:)

Research grants in the occupational health area include studies in the use and evaluation of modern methods of testing pulmonary function in miners and others who have lung diseases resulting from dust inhalation. Other studies are being made of the mechanisms of action and factors influencing the absorption, distribution, and elimination of occupational toxic agents such as mercury, lead, and organic solvents. Several studies are being supported in the evaluation of noise in the working environment, the detection of noise susceptible individuals, the reduction of noise and other methods of protecting the individual. Other studies are being made of the effects of exposure to vibration and to heat.

INCREASE FOR DIRECT OPERATIONS

Mr. FOGARTY. In your direct operations you are requesting an increase of $155,500 and six positions. What is this for?

Dr. MAGNUSON. $50,000 of that, sir, is for the uranium miners' study. The rest of that goes for the annualization of the program this last year—$116,500 for annualization.

Mr. FOGARTY. You only have six positions, I see. Annualization would take what?

Mr. ACKERMAN. The annualization, of course, is the full-year cost of the program that was begun in 1961. The figure here is $116,500.

Mr. FOGARTY. That is the big part of that increase, then.

Mr. ACKERMAN. Yes, sir.

HEALTH HAZARDS IN URANIUM MINING

Mr. FOGARTY. On page 175 you say that the levels of radiation in two-thirds of the uranium mines which have been observed are in excess of the recommended levels. What have you done about it?

Dr. MAGNUSON. We have been trying, through the State agencies, to call this to the attention of all of the interested groups. One of the important things that was done this last December was through the Department and through the Secretary. A conference was held with a number of the Governors of the States which are involved in the area to bring this situation to their attention. We have been giving a large number of training courses for mine operators and mine inspectors in the Colorado Plateau area. We have developed certain kinds of educational material that we and the Bureau of Mines are using to get to the miners themselves, since we found that even where adequate control measures had been introduced sometimes our purposes were defeated by the man not understanding the importance of these measures.

We have been able to do some stepping up of this activity this last year. The amounts requested in the budget for next year will permit us to intensify this work.

Mr. FOGARTY. With what you are going to have to work with next year, will you be able to bring this down to the recommended levels?

Dr. MAGNUSON. It will allow us to make a start. That is about all I can say, sir.

Mr. FOGARTY. I think you can answer that question better than that. Either you can or you can't.

Dr. MAGNUSON. I believe that we could profitably use a good deal more in this activity, sir. As a program operator, I feel that this is an important area and one which we do need to intensify.

Mr. FOGARTY. That is a pretty serious thing to say in the justifications—that two-thirds of the mines are unsatisfactory. Isn't that about what you said?

Dr. MAGNUSON. That's right.

Mr. FOGARTY. With the money that you have available today, you are still going to have men working in mines which are not safe as far as the standards that you have developed?

Dr. MAGNUSON. Right.

Mr. FOGARTY. I am wondering if we ought to give you more money, or make a list of the mines public. Wouldn't that be a good thing to do, publicize the mines?

Dr. MAGNUSON. I don't think that would solve the problem, sir.

Mr. LAIRD. Why wouldn't it help?

Dr. MAGNUSON. It might. But the difficulty that one has here is that for action to be effective, it requires the understanding and the help of everyone involved, not only the owner of the mine but also the miner working down at the face of the mine. There is more than a legalistic approach to this thing; even though one might have it in the background to fall back on as a last resort.

Fundamentally, I think we do better by driving home to the owners and to the miners themselves these points: this is serious business, this is what can be done, and here is how to do it.

BUDGET REQUESTED FOR 1962

Mr. FOGARTY. For occupational health, what is the full amount that you have budgeted for 1962?

Dr. MAGNUSON. The full amount that we have for 1962, sir, in the President's budget is $3,981,000—of which $1,884,000 is for grants and just over $2,097,000 for direct operations.

Mr. FOGARTY. What did you originally request?

Dr. MAGNUSON. The Public Health Service request——

Mr. FOGARTY. Your request to the Public Health Service.

Mr. ACKERMAN. The Bureau of State Services requested $4,755,000.

Mr. FOGARTY. What did the Public Health Service request?

Mr. ACKERMAN. The same amount.

Mr. FOGARTY. So you were cut about $800,000.

Dr. MAGNUSON. Yes, sir.

Mr. FOGARTY. Where was that $800,000 cut made?

Mr. ACKERMAN. It was just about half and half—the Budget Bureau and the Department.

Mr. FOGARTY. Will you put in the record the breakdown of that $800,000 and the positions, and how you were going to use it.

Dr. MAGNUSON. Yes, sir.

Environmental health activities—occupational health, 1962

Program activity	Preliminary estimate		Bureau of the Budget allowance		Reduction	
	Positions	Amount	Positions	Amount	Positions	Amount
Grants: Research		$1,884,000		$1,884,000		
Operations	255	2,871,000	183	2,097,000	72	$774,000
Research	158	1,820,000	105	1,188,000	53	632.000
Training	21	239,000	15	193,000	6	46,000
Technical assistance	76	812.000	63	716.000	13	96,000
Total	255	4,755,000	183	3,981,000	72	774,000

The original request of the Public Health Service included an additional $774,000 and 72 positions which did not appear in the budget submitted to the Congress. These requests were in the following areas:

1. Research	$632,000
2. Training	46,000
3. Technical assistance	96,000

Research which would be supported by these funds is directed primarily to the problems of toxicologic testing described in the opening statement and the testimony following the opening statement. This would include funds for the acquisition of personnel, equipment, and materials to begin an evaluation of physiological and psychological measurements of the effects of chemicals on experimental animals. This would include, but not be limited to, the so-called performance testing referred to in the testimony. It is most important that the investigators and others in this country have an opportunity to evaluate the reality and significance of testing procedures in order that results from European centers can be equated with our experience.

To the extent that knowledge develops from these experiments in animals and to the extent opportunities arise, such physiologic and psychologic measures will afford test measures that can be applied directly to man in the work situation providing needed checks on our own recommended safe levels of exposures.

Six positions and $46,000 were requested to expand and intensify our training efforts in the field of occupational health. Our short-term training courses designed to increase the competence of State and local health and labor department personnel have been enthusiastically received for years. However, each year we have turned down a number of personnel requesting this type of training because of our limited resources.

In addition to presenting our short-term training courses for chemists and industrial hygienists our training program would have been expanded to develop training courses for nurses and physicians.

Thirteen positions and $96,000 would have enabled us to increase our program of assisting the States to develop and improve their occupational health activities. In addition to increasing our consultative efforts to the States, these funds would have provided for the assignment of personnel to these States that are in critical need of experienced workers.

MOST PRESSING NEEDS

Mr. Fogarty. If you had this $800,000, where would you put the biggest part of it? What are your most pressing needs and problems right now?

Dr. Magnuson. The one that is certainly the most pressing and the one—in spite of any other long-range conditions—we have to give immediate attention to, is this uranium miners' problem.

Mr. Ackerman. I might say that this had not come to a head at the time the preliminary estimates were made. Actually, that was not a major factor in this request.

Mr. Fogarty. If it hadn't come to your attention at that time, instead of $800,000 more, what do you think you actually ought to have?

Dr. Magnuson. We have had some discussions within the Public Health Service, and we believe an additional $300,000 will be required for the uranium miner work.

Mr. Fogarty. At the time of your original estimate of $800,000, this problem had not come to a head.

Dr. Magnuson. That's right.

Mr. Fogarty. In addition to the $800,000, what do you think you could use or need because of this problem coming to a head, $300,000 more?

Dr. Magnuson. Yes.

Mr. Ackerman. Of course we have $50,000 in the budget for this purpose.

Mr. Fogarty. So you think you need about $1,100,000 more in the budget. Is that right?

Dr. Magnuson. Yes, sir.

Mr. Fogarty. Mr. Denton?

COOPERATION WITH OTHER AGENCIES

Mr. DENTON. How does the work which you are doing conflict with work performed by the Bureaus of Mines and Labor Standards?

Dr. MAGNUSON. We work very closely together, sir, and are almost in constant contact. To take them up separately, the Bureau of Labor Standards is given the primary authority for the prevention of occupational accidents which relate to accident problems such as a man sticking his hand in a saw or something like that. We are given the primary responsibility for the prevention of occupational diseases due to exposure——

Mr. DENTON. Does that cover use of masks?

Dr. MAGNUSON. The masks, sir, are a peculiar thing. Actually, the testing of masks is in the Bureau of Mines. They do all the testing of masks at their experiment station in Pittsburgh. The Bureau of Mines has the primary responsibility for the occupational safety in the mines. We work very closely with the Bureau of Mines.

For example, in these silicosis——

Mr. DENTON. I am on the committee that makes appropriations for them, too. We had this same problem up there.

Dr. MAGNUSON. May I explain how we work with the Bureau of Mines, sir?

Mr. DENTON. Yes.

Dr. MAGNUSON. The silicosis study is a case in point. The Bureau of Mines in the silicosis study has been doing primarily the environmental studies. They have been making the dust measurements, the study of mine ventilation. We have been doing all of the medical studies. The way this has worked out, the Bureau of Mines' team goes into a mine and our medical team comes in anywhere from 2 weeks to 2 months later, depending on the schedule, to examine the miners.

We are coordinating this study through a committee between our two groups.

Mr. DENTON. You don't work with the Bureau of Labor Standards?

Dr. MAGNUSON. Yes, sir. We work closely with the Bureau of Labor Standards. We work with them, for example, in the development of joint kinds of publications. The Bureau of Labor Standards is the one that has the responsibility for running the President's Conference on Occupational Safety.

Mr. DENTON. That includes occupational diseases, too, doesn't it?

Dr. MAGNUSON. That's right. We worked with them on the last conference and were a part of the planning committee in developing the program, and so on.

Mr. DENTON. You don't think there is any overlapping, but it is coordinated work?

Dr. MAGNUSON. I honestly don't believe there is any overlapping. Our relations are the most cordial, and they are meeting with us and they are inviting us to meet with them and their State counterparts.

Mr. DENTON. I am on two committees which make appropriations for at least three different agencies in the Government that are dealing with this particular problem.

Dr. MAGNUSON. Parts of it; yes, sir.

Mr. DENTON. I think that is all.

STUDIES OF AGRICULTURAL WORK HAZARDS

Mr. Laird. You talked about this study that you are making on silo fillers disease. What other work are you doing on agricultural diseases?

Dr. Magnuson. A number of things. We are involved right now in a study of the potential hazards in feed mill operations. You are undoubtedly familiar with the way these feed mixes are made up in a number of small mills throughout the country.

At the present time there are something like 100 additives which various people are adding to these feeds, ranging all the way from some very powerful hormones to such things as arsenical compounds and so on. We are in the midst of a study here to determine whether there are any health hazards associated with this operation.

We have been in the middle of some work on the hazards in the handling of castor bean pomace, which is the dried part of the castor beans after you extract the castor oil. Some of these materials are very strong sensitizing agents. There is some grant money going into the study of infectious diseases in agriculture.

Mr. Ackerman called my attention to another study that I should mention. This was a study of a new dermatitis occurring in the celery industry. This was primarily occurring up in Michigan. The harvesters of this celery were developing a perfectly frightful dermatitis, with great big blisters on their skin. Our dermatologists were able to trace it down to a chemical that was being produced by a fungus growing on the celery which caused a disease of the celery known as pink rot.

This chemical was getting on the workers' skin, and then when the workers' skin was exposed to sunlight it caused a very severe type of skin lesion that looked like poison oak or poison ivy.

COOPERATION WITH NIH

Mr. Laird. How closely are these projects checked with the National Institutes of Health?

Dr. Magnuson. Very closely checked.

Mr. Laird. There were some grant projects at the National Institutes of Health dealing with the same area as far as allergies are concerned. This last one you discussed is in the area of allergies. Are these research projects brought to your attention?

Dr. Magnuson. Yes, sir.

Mr. Laird. You are familiar with the projects at the National Institutes of Health?

Dr. Magnuson. Yes.

Mr. Ackerman. I may say, Mr. Laird, that liaison with NIH has been greatly strengthened this year because of a transfer of research grants from the National Institutes of Health to the Bureau of State Services' appropriation in Dr. Magnuson's program. This has required joint teams to be working with NIH in review of these grants; so I am sure the liaison with them in the research field is much stronger and closer than it has ever been.

Dr. Anderson. I might say on that point, Mr. Laird, that all of the grant applications come into one place in the Public Health Service, where they are reviewed by one staff. As aids to this staff, each of the programs in the environmental health area has designated a person to participate in the discussions at this central receipt and assignment point. So they know what is coming in and they know to whom it is being assigned, and they can watch for the reports and progress and so on.

SILO FILLERS' DISEASE

Mr. LAIRD. These programs are becoming so big that I have the concern that perhaps we are overlapping our efforts sometimes. You take, for instance, this area of silo gas. Most farmers that I know are very well aware of the problem of the silo gas. There are a few who perhaps make a mistake once in a while, and they have accidents. But isn't it true that most farmers are pretty familiar with this problem?

Dr. MAGNUSON. How does one define "most"? The fact is, we still run into these kinds of accidents. These things do happen. Through research work such as this—and this is a research grant through which we carry this on—methods are being found so that these gases will not form.

Mr. LAIRD. Our State department of agriculture sends out information to these farmers about the danger of silo gases. You see it in the local newspapers. Last year at silo-filling time there were warnings in all our local papers about this. I remember it very well. I just wonder how far you can go in carrying out your responsibilities as far as filling silos is concerned.

Dr. MAGNUSON. We are faced with this kind of problem all the time in public health, and that is, you make knowledge available as you can, regardless of how many people follow your advice. There are always going to be people who do otherwise.

What such research does is to develop—shall we say—more foolproof devices and additional safety measures.

Mr. LAIRD. We make all this information available. Is it necessary for the Federal Government to be the keeper of every farmer?

Dr. MAGNUSON. I don't think it is.

Mr. LAIRD. How far do you want to go on this type of a program?

Dr. MAGNUSON. Taking the silo fillers' problem, this is a situation where a group of investigators at the University of Wisconsin, I believe, put in this research grant application to study this disease known as silo fillers' disease. It was recognized that indeed such accidents happen. These men had what was a germ of an idea here of developing knowledge of the cause of the disease and developing a method of control.

Mr. LAIRD. I am not talking about the research. I can see where you have a responsibility for research. But I thought you were talking about a little different responsibility in this area—that you were getting into the area of seeing that the farmers didn't get into these silos.

Dr. MAGNUSON. No; this was strictly a research project.

Mr. ACKERMAN. Dr. Magnuson was answering Mr. Fogarty's question as to what this research grant money was producing.

Mr. LAIRD. You were just addressing yourself to the question of research?

Dr. MAGNUSON. That's right.

COOPERATION WITH OTHER AGENCIES

Mr. LAIRD. You make the statement that two-thirds of the uranium mines are not safe for the miners. You know why they are not safe. Isn't that correct?

Dr. MAGNUSON. Yes, sir.

Mr. LAIRD. You have notified the mine operators about how to prevent the problem that does exist in these mines, and you have also notified the miners. Evidently nothing has been done in two-thirds of the mines. Is that correct?

Dr. MAGNUSON. Yes, sir. I hesitated on that answer—if I may explain, Mr. Laird—because it depends on how you group these two-thirds. Our most difficult problem right now exists in the smaller mines. There are large mines that have extensive ventilation facilities and small mines that have none.

Mr. LAIRD. We have the Bureau of Mines; we have Labor Standards; and we have you in this particular area. Who should have the responsibility as far as seeing that these mines are safe?

Dr. MAGNUSON. The present interpretation of the legal side of this, as I understand, sir, is that the ultimate responsibility for the control of these rests with the several States and does not rest either with the Public Health Service, with the Bureau of Mines, or with the Bureau of Labor Standards.

Mr. LAIRD. Yet we have three different Federal agencies in this particular area. You must spend a lot of time just meeting with these other two agencies, don't you?

Dr. MAGNUSON. We stay pretty well in touch with each other.

Mr. LAIRD. Do you think anything would be gained by having one agency responsible for this type of work on the Federal level?

Dr. MAGNUSON. My own feeling, Mr. Laird, is no.

Mr. LAIRD. You talk like the Army does as far as the space program is concerned. I was listening to the Defense hearings the other day, and the Army really can't see any reason why this new order of the administration should be implemented because they feel that having three groups in the same field works out pretty well.

But now I am trying to find out why you don't think having one group would work out well in this area.

Dr. MAGNUSON. The reason I feel that way, Mr. Laird, is this. One is dealing here with three very different kinds of competencies. We contribute to this segment of the problem a high degree of medical and industrial hygiene engineering competence—a competency of medical scientists, a competency in epidemiology, and so on, which the Public Health Service has and which the other agencies do not have.

The Bureau of Mines contributes the kind of thing that we are not expert in—for example, what is the best way to design a mine ventilating system to do such and such? We make no pretense at being expert in this field.

The Bureau of Labor Standards comes into this area because they are particular legal experts as it relates to certain provisions of the Walsh-Healey Act. How far does the Walsh-Healey Act go in this particular case? This is a legal approach that is a Department of Labor competence, a Department of Labor responsibility.

If there were a real conflict among these agencies as to who is doing what here, I would be inclined to agree with you. But here we have an overlapping of various kinds of professional competence coming into the problem, and I think we are working very well together.

RECENT DETERMINATIONS

Mr. **Laird**. You say this problem, as far as the uranium mines, was brought to a head rather recently?

Dr. **Magnuson**. Yes, sir.

Mr. **Laird**. When was it brought to a head?

Dr. **Magnuson**. We realized when we went into this study that, based on our experience, there would have to be 15 or 20 years' experience accumulated before the final pattern became known. We are in our 10th year, as I said earlier.

What brought this to a head this last summer was the findings of our triennial examination of these miners. Three years ago and again this last summer we used some new tests that are very sensitive indicators of changes in cells.

The expert cytologists at the Cancer Institute who work with us on this thing tell us these tests are highly suggestive that these men are either now, or immediately will be, candidates for lung cancer.

When the results on last summer's examination started to come into us this fall, there had been a tremendous change over the 3-year period. This made us realize that this was probably an additional forewarning to us that our time was running out.

Mr. **Laird**. So you think this is a substantially new program you are talking about now?

Dr. **Magnuson**. I think it is certainly an accelerated and an increasing program.

REASON FOR NOT REQUESTING BUDGET AMENDMENT

Mr. **Laird**. Why didn't this meet the requirements of the Secretary's budget?

Mr. **Kelly**. It was not presented. There was nothing on this problem which was brought to the Secretary's attention.

Mr. **Laird**. Why wasn't this brought to the Secretary's attention?

Dr. **Anderson**. The Secretary called this conference of Western Governors in December, at which time he outlined to them the problem; and the responsibilities of the various agencies within the States were discussed.

The Public Health Service offered what help it could to the States in achieving some control of this problem in the miners, because we were very much concerned about the health of these people. Some of these miners move from State to State, for example, and engage in the same occupation in other States and contribute to the load that is experienced in various States with regard to workmen's compensation.

As Dr. Magnuson said, some of these problems are related to the silica hazard in some of these mines. So the problem was discussed with Secretary Fleming; and, as a consequence of this discussion, in December or late November there was put into the budget request before you a designation of $50,000 to accelerate the program somewhat.

Mr. Laird. That was all that was asked for though.

Dr. Anderson. No. We talked in terms of the needs of this program as being in the magnitude as Dr. Magnuson has mentioned.

Mr. Laird. Where was it cut from $300,000 to $50,000?

Dr. Anderson. By that time the overall ceilings for the Department's request had been pretty well jelled.

Mr. Laird. Why wasn't this presented when the budget amendments were asked for by the new administration, then?

Mr. Fogarty. Mr. Kelly will have to answer that. He has a stock answer to that question.

Mr. Kelly. I indicated to you that we issued the instructions under which the Surgeon General was acting. In the total environmental health field, the 1962 budget before you contains a 20-percent increase as compared with 1961, taking into account the additional funds that Congress made available in 1961. It is about 85 percent over 1960, and the Surgeon General did not include this as one of the areas that he felt met the test of the guidelines that we gave him.

Mr. Laird. In other words, the new administration felt that this was adequate.

Mr. Kelly. That is correct; yes.

Mr. Laird. I wanted to get that cleared up because I think if this was just something that came to a head in the last week or so, it might have been too late. But it wasn't just in the last week or so.

Mr. Kelly. Not to my knowledge.

Mr. Laird. That is all I have, Mr. Chairman.

Mr. Fogarty. Mr. Michel?

Mr. Michel. No questions.

Mr. Fogarty. Do you have anything else you would like to say, Dr. Magnuson?

Dr. Magnuson. No, sir.

Radiological Health

Mr. Fogarty. Next is radiological health activity. Go right ahead, Dr. Weber.

Dr. Weber. Mr. Chairman, I have a statement to file for the record, and a short summary which I will read.

Mr. Fogarty. We will place your prepared statement in the record at this point.

(The statement referred to follows:)

Mr. Chairman and members of the committee, the problem of ionizing radiation has grown from a small special one, virtually confined to the use of X-rays in the healing arts by a numerically limited group of more or less knowledgeable scientists and practitioners, to one that is now a general problem for society involving every aspect of its structure. This growth has not only been rapid, but owing to the atmosphere of secrecy with which important defense activities had to be conducted, the problem of ionizing radiation has developed without society being aware of its presence. As a result, the comprehensive effort necessary for public health protection from such radiation has been greatly delayed in this country. This fact has been pointed out to the Surgeon General by the National Advisory Committee on Radiation. Such a state of affairs has resulted in an administrative handicap in initiating public health efforts, which is aggravated by the deficits in knowledge concerning the effects of low-level exposure to the human population. This has posed serious questions about what standards need to be enforced for the health protection of the population from proximal or distant sources of various levels of intensity, and reduces most operational procedures to reliance on educated guesses. This situation can be improved only by a well-integrated public health research effort, which must be primarily concentrated on the only place where the whole matter can be finally decided—the human population. All other efforts must be related to this.

The few epidemiological studies which have been conducted on human populations—effects on radium watch dial painters, medical exposure leading to variable and usually disputed degrees of genetic and somatic damage—are all too few. None of them are considered complete in terms of sufficient numbers of subjects studied or adequacy of techniques to elucidate important points necessary for adequate understanding of radiobiological effects. This is a task of great difficulty since it requires the presence of closely coordinated public health task forces with expertise in epidemiological methods, accompanied by adequate laboratory support to examine major details of the whole problem which experts meet in the field. In this area the biological variables are so many that a research program becomes multidisciplinary as well as interagency coordinated. Indeed, radiological health is not a single specialty, but rather a series of specialties sharing a common public health approach, with emphasis on the discernment of the effects on human population as well as the means by which adverse effects can be diminished or eliminated. There exists this need for public health research encompassing radiological biology, which is a special field of study emphasizing work calculated to improve the interpretation of biological effects stemming from low and intermediate level exposures from combined sources in population groups, general and special. Therefore, we must now direct our attention toward meeting outstanding extant needs in specific areas. Efforts in these respects must be directed as follows:

RESEARCH

1. *To assess population exposure from all sources of ionizing radiation.*—This is a first step in order to discern more clearly the extent and the kind of radiation exposures that exist. Therefore, adequate data on radiation exposure sources, as well as their levels, correlated with body burdens which originate as a result of cumulative exposure, are a necessity in nearly every aspect of the radiological health program. Various data collection networks (i.e., air, water, milk, etc.) are producing parts of the total needed data. It is now essential that there be a more integrated approach in existing data collection activities, with the work extended to include presently untouched areas (such as total diet). The current effort to develop a radiation intelligence network will, when completed, achieve this goal.

The data gathered and analyzed by the latter will represent a combination of existing radiation data from various sources, and will permit establishment of a radiation index for as many as 80 different geographical areas of the country. It is believed this technique will produce a clearer picture of radiation exposure for any geographical situation for any individual on virtually any one day; treated in terms of average exposure to radiation from all sources, whether environmental or medical, natural or man made, and by such categories as sex and age. The critical nature of the need for this type of information is highlighted by the latest recommendation of the National Committee on Radiation, which stated that exposure of the general population from manmade sources (excluding radiation in the healing arts) of radiation exposure could not exceed that resulting from natural background. Therefore, a system of intelligence is needed for the dual purpose of (1) determining whether this health standard is being met, and (2) to guide the direction of special, applied reduction efforts where safety standards are being approached or exceeded.

Therefore, in fiscal year 1962 the proposed increase of $211,400 will help develop this project from its present pilot operation to the beginning of the basic, integrated, radiation intelligence system which is need.

2. *To develop the technical basis for relating the effects of environmental, occupational, nonoccupational, and medical radiation exposure to large population groups.*—Since the discovery of the X-ray in 1896, exposure of the population from this and other radiation sources has been on the increase, marked by acceleration during the past several years with no signs of diminution in the foreseeable future. In addition to natural background radiation (cosmic rays entering the earth's atmosphere and natural radionuclides in the earth's crust), the curve of external exposure from X-ray and gamma radiation has risen, and the living environment containing such media as soil, air, water, including both domestic water supplies and that of the seas, has come to contain

more than normal amounts of radiation. This is reflected, for example, in an increased deposit of radioactive materials in the human body due to the entry of increased amounts of radioactive materials into the food chain. Therefore, techniques must be developed to determine the effect of this on exposed population groups in terms of specific conditions in which, at least in certain amounts, radiation exposure is known to give rise.

As part of the requirements, we have initiated studies on congenital malformation, possible untoward results from X-ray pelvimetry, and where a high number of deaths from leukemia have been noted, the possibility of an associated radiation factor. In addition, a cooperative project has been undertaken with 15 university and medical centers to study the dose-effect relationship from the use of iodine–131 for treatment of thyroid diseases. It is believed that this useful medical agent (probably the most widely used of the radionuclides in medicine) is capable of cancer or leukemia induction, and hence needs to be examined apropos the population groups in which it has been employed.

3. *To develop scientific criteria for evaluating the effects of radiation exposure on health—that is, to develop a scientific basis as support for Federal Radiation Council and other national decisions on standards of radiation exposure for the general population.*—The most important practical problem today centers about the scientific basis for standards of exposure. One of the practical reasons is the need to know what degree of ionizing radiation can be imposed, a matter both of health as well as one with important socioeconomic implications. Because of its dangerous effects, some scientists would virtually eliminate all artificially produced radiation. There are all grades of opinion ranging from that extreme. The imposition of controls strict enough to satisfy the doubts of all would price out of existence otherwise useful and powerful sources of energy. Unfortunately, the lack of sufficient knowledge, attended by difficulties in correlating the data that now exist prevents any unanimity of agreement as to where the balance of benefit versus risk should be struck.

Therefore, in charting the Public Health Service research effort, it has been necessary to establish a special research evaluation and planning activity designed to assure that integration, balance, coordination, and continuity are built into the research program. The acquisition of an outstanding scientist as Chief of the Research Branch in the Division of Radiological Health has given the research program a new impetus. Dr. Paul C. Tompkins, former Scientific Director of U.S. Naval Radiological Defense Laboratory at San Francisco, Calif., and a recognized international authority in the field, was named Chief of the Research Branch in July 1960.

4. *To develop methods for predicting public health implication based on full knowledge of present and proposed programs of nuclear technology and medical uses of radiation.*—Although it is true that medical sources of radiation currently constitute the greatest source of manmade radiation exposure, and will probably continue to lead the others for some time to come, the picture is changing with respect to this. In addition, there are new sources which pose their own peculiar risks. For example, nuclear-propelled space rockets and other atomic power sources, capable of operating electronic and communication devices for extremely long periods of time, are now being constructed. These contain the potential for different kinds of external and internal exposure problems. Other developments include atomic-powered vessels and aircraft as well as an expanding number of nuclear power and experimental reactors. Radiation techniques, already found to be useful in diagnosis and treatment of illness, with more to come, and similar devices of proven value in industry and elsewhere are adding their increments to population exposure. Consequently, a significant part of the Public Health Service's program in the ionizing radiation field needs to be concerned with the contributions made by these devices to the total picture. This requires the application of techniques, some now at hand but not yet generally applied, plus development of new techniques for aspects of the problem not yet manageable.

5. *To develop, demonstrate, and promote public health methods for radiation exposure reduction and control.*—One of the first steps in this program area was taken with the inauguration of a practical system for the statewide survey of dental X-ray machines, calculated to disclose any defects which may cause unnecessarily heavy exposure to patient and operator. The system combines the features of a complete "mail-order" survey packet and the use of specific safety devices for the reduction of exposure to patients and technicians. This new procedure has now been tested in four States in cooperation with dental

associations. Additional requests have been received for its extension to 20 more States in which are located approximately 28,000 dental X-ray units, or nearly one-third the number of an estimated 90,000 such units in use in the United States.

The next major project to be started is the development of a method for reduction and control of radiation exposure from medical X-rays. It is believed that such procedures as the chest X-ray, probably the commonest form of medical roentgenographic examination will lend itself as readily as dental roentgenography to a similar approach. Also, in this area is a project to develop rapid and economical methods for the removal of strontium 90 from milk in the event that certain situations should call for the application of such reduction methods. This project is being conducted in cooperation with the Department of Agriculture and the Atomic Energy Commission.

6. *To conduct a national program of long-range and short-range applied and fundamental research to support and implement the missions previously described.*—The overall situation has been surveyed to determine the principles which need to be followed in working out techniques to achieve such a program. In working toward this goal, the Division of Radiological Health emphasizes the epidemiological approach which centers about the study of the varying patterns of disease affecting the human population. The conduct of such work entails both a field effort with examination of human population groups as a central part of the effort, as well as necessary laboratory activities conducted in close association with such examinations. In addition, of course, all of the data that may bear on these problems and which may have been developed by other students in the radiological sciences are correlated with the ongoing investigations. Certainly, all of these things are needed for a correct evaluation of so complex a problem, and particularly if one is to make reasonably rapid progress toward a better understanding.

Fortunately, it has been possible within the past year to make a start in this work. Such studies as the followup of the human population exposed to certain ionizing radiation agents on the Animas River, the beginning of work on iodine 131 patients already mentioned, the field investigations on the movement of radioisotopes through the environment being conducted in several parts of the country, the study of populations with a record of special exposures to medical X-rays, as well as a number of others have been initiated. All of this is being related to on-going laboratory research within Public Health Service facilities. This includes the intensified work at the Sanitary Engineering Center at Cincinnati, Ohio, and that started through the acquisition of two new laboratories at Montgomery, Ala., and Las Vegas, Nev. It is now being added to through facilities which have come into being within the past several months in Montgomery County, Md. Basic laboratory procedures like tissue culture work, molecular biology and histopathology, all needed as a tie-in with basic fieldwork, have been established or are in process of establishment. Since this approach also requires suitable animal studies, the 1962 work plan makes provision for such studies.

RESEARCH GRANTS

Research grants are also being utilized to secure the benefits of nondirected research efforts by the scientific community of the country. This permits us to make use of the competencies and facilities available at university and medical research centers to augment our own direct research efforts.

TRAINING

To reduce the shortage of trained manpower in the radiological health field.—The discipline of radiological health is not a single discipline, but rather is a series of professional and scientific disciplines. This means that on the public health side one needs not only the traditional public health physician and the sanitary engineer trained in the health sciences, but also the nurse, the health educator, the veterinarian, the radiologist, the dentist, as well as others. On the side of the basic sciences are needed radiochemists, physicists (especially the health physicist), radiobiologists, and individuals trained in a variety of disciplines fundamental to the nuclear sciences. Needless to say, as various well-documented studies have indicated, there is a considerable shortage of trained manpower in each of these specialties and, of course, in the grand total needed now and in the future.

Fortunately, it has been possible to undertake during the current fiscal year a categorically designated program to develop radiological health specialists through the $500,000 appropriated by the Congress for grants to universities and other educational institutions for the training of these specialists. As part of the mechanism for handling this grant program, a committee was established composed of present and former members of the National Advisory Committee on Radiation, to review grant applications and make appropriate recommendations to the Public Health Service. At the first meeting of this committee in November 1960, 20 grants, totaling nearly $1 million, came up for consideration. Inquiries received from interested educational institutions indicate that additional grant applications can be expected during the next few months. Therefore, the program is well oversubscribed, an indication of the interest and capabilities of outstanding educational institutions to supply the manpower needs of this field.

Other aspects of the fiscal year 1962 training effort will include continuation of graduate academic training of selected service officers, as well as an expansion of the program of topical short courses for State, local, and Federal health personnel. To date, these courses have been conducted mainly at the Sanitary Engineering Center in Cincinnati. During 1962, however, the latter will be supplemented by a number to be held at such places as Montgomery, Las Vegas, and Rockville, where the additional facilities are providing opportunities for such expansion.

TECHNICAL ASSISTANCE

To continue efforts to expand the role of the States.—Up to this point our remarks have centered about some of the pressing areas of need which can be met effectively only at the Federal level. This does not mean that the primary responsibility, legally borne by the States, for the application of sound programs to protect the public from unnecessary radiation hazards goes unrecognized. On the contrary, this principle is a basic operating tenet of any Public Health Service program. It only remains to reemphasize that which I have narrated in previous testimony, that we shall continue to allot a substantial part of our activities to the area of providing technical advice and assistance to State health authorities in the development and conduct of their programs. Therefore, in fiscal year 1962 we will continue our work in this area through technical and professional staff stationed in our regional offices, the direct assignment of selected staff members to various State health departments, the provision of laboratory services and support for needed supplementation of the States' programs, and expanded efforts in such joint programs as X-ray surveys, field investigations, and others.

The amount requested for this program in 1962, $9,147,000, is an increase of $1,487,000 over 1961 of which $280,000 is for research grants and $1,207,000 for these other planned activities.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Dr. Weber. Mr. Chairman and members of the committee, for many years after the discovery of the X-ray in 1895, ionizing radiation affected only those comparatively few professionals using or exposed to X-ray. However, great changes have occurred which affect all society directly and insidiously. New sources of ionizing radiation have appeared as a result of atomic fission. At the same time, the older sources, like the X-ray which marked the beginning of man-made sources, have increased in number and power and in usage.

Since undue radiation exposure can be harmful, strong and effective public health programs for population protection are needed if the value of these powerful agents is to be realized. In short, the problem is here; it is big and will get bigger; it is complicated and will require large-scale efforts; and the public health program which is needed is just beginning.

RESEARCH

A sound public health program requires a research effort of sufficient scope to determine what constitutes significant exposure to the population as a whole, as well as to the different individuals within it; a governmental administrative framework—Federal, State, and local—to make possible reliable radiation protection programs; and a special training effort to make certain that the trained technical manpower to carry out these proposals is available.

Let us first consider our research effort. First, we must know the sources of radiation exposure in the environment and then the degree to which such sources, singly or in combination, are affecting the population. Collection networks to sample air, water, milk, and food have been developed. When the network system is perfected, we shall have an index of radiation exposure for about 80 different geographical areas of the country. This is an urgent priority for the analysis and interpretation of data on environmental radiation levels.

This requires supporting laboratories where we can analyze the environmental samples collected by the network system. Within the past year three new laboratories have been established: At Montgomery, Ala.; Las Vegas, Nev.; and in Montgomery County, Md. In addition to sample analysis, all of the modern scientific laboratory procedures like tissue culture work, molecular biology, and animal studies are being used to evaluate the effects of exposures more precisely.

The next step in research aims to assess the degree of injurious effects to the population exposed to various levels of radioactivity. In seeking ways to assess radiation damage, we have initiated studies of congenital malformations which might be caused by unusually high levels of natural radiation found in certain areas. We are investigating the incidence of defects in children whose mothers were exposed to abdominal X-ray during their pregnancies. We are checking environments where deaths from leukemia have been relatively high; we are also looking for untoward effects from iodine 131, the widely used radionuclide of medically proven value in the management of thyroid diseases, through a study of patients treated with this radionuclide in 15 medical centers.

Other studies include the examination of people living on the Animas River in New Mexico, who have over the years drunk water containing an excess of radioactive material from industrial waste discharges into the stream. Other studies seek to determine the degree of increased amounts of radiation exposure in the food chain, and the factors which enter into the movement of such materials through this food chain. All of these efforts concentrate on radiation problems in the human population, because this is an area of special Public Health Service responsibility. This demands extensive observation of large human population groups.

The next special research effort is designed to permit establishing standards of exposure on a more exact basis. Present data are insufficient to clearly delineate standards for low levels of exposure. We are seeking the scientific facts necessary to make more precise formulations. A special unit of experts has been established for this important activity.

The research program will give particular attention also to newer applications of radiant energy which pose their own peculiar risks. These include nuclear-propelled space rockets, atomic-powered electronic and communications devices, nuclear-powered vessels and aircraft, as well as an expanding number of stationary nuclear reactors. To evaluate and control the hazards of these applications requires new and different techniques based on the novel problems each presents. However, we can determine these risks only when there has been actual field experience with them.

Another aspect of research concerns methods for insuring safer operation of X-ray equipment. The Division has already developed a successful method for detecting dental X-ray machines that are operating dangerously. We are now working on practical and effective methods for medical X-ray machine examinations.

Another example of our efforts to reduce exposure from radioactive materials is our work in cooperation with Atomic Energy Commission and the United States Department of Agriculture, in which we are seeking rapid and economical methods for removal of strontium 90 in milk.

The radiological health budget for the first time provides for an extramural research grant program which has been transferred from the National Institutes of Health. This should better enable the Division to secure the benefits of the nondirected research contributions of the scientific community of the country. As such, it augments the Division's efforts.

TRAINING

As in virtually all of the newer technological fields, there is a considerable shortage of radiological health manpower. The National Advisory Committee on Radiation has vigorously urged action to provide training programs to overcome this shortage. This field is not manned by a single specialty, but rather by a number of scientific specialties oriented about a common public health approach.

During the current fiscal year the $500,000 appropriated for grants to educational institutions has made possible a new program to train radiological health specialists. The response to this program has been enthusiastic, to judge by the 20 applications from as many universities, considered by the training grants committee in the fall of 1960. This, as well as the continuing program of short-course training and the graduate academic training of selected service officers, will, we feel, soon begin to make some inroads into the national personnel deficits in this field.

TECHNICAL ASSISTANCE

However, research findings mean nothing if they are not put into operation. The aim of our technical assistance activities is to help those who have important responsibilities for protecting the health of citizens from ionizing radiation. Therefore, this part of the program is being strengthened in order to assure that no area will lack at least minimal services for necessary preventive and corrective measures. The dental Sur-Pak program is a good example of how we go about this.

I would like to make a special point, Mr. Chairman, of the dental X-ray program because of its success.

THE CONTROL OF DENTAL X-RAYS

Surveys so far conducted indicate that some 75 percent of all dental X-ray machines in use in this country subject patient and operator to unnecessary radiation exposure, in most cases due to correctible defects in the equipment. The Sur-Pak method, developed by our staff, is designed as a simple and inexpensive method of locating and defining these defects so that corrective steps can be taken.

Basically, the Sur-Pak consists of a 9-inch by 11-inch envelope into which is sealed an 8-inch by 10-inch X-ray film on a lead-backed exposure holder. Complete instructions and a self-addressed return envelope are included. This packet is sent to cooperating dentists, through the State health departments. The dentist exposes the film to his X-ray unit's beam; places it in the self-addressed envelope; and mails it back to the health department. The health department returns the Sur-Paks to us in groups of 50 to 100 for processing.

Here are examples of three films from Sur-Paks we have recently received from Missouri. We get a beam about this diameter, which is like the small Sound-Scriber disk. This is the normal size beam, the recommended size, which meets the recommendations of the American Academy of Oral Roentgenology—2¾ inches in diameter.

In addition, I have two of the three actual films, which show larger diameters. The big one is here. This is the normal size Sound-Scriber disk which gives you an idea of the beam from this particular machine—a beam which is too big. I have the second one here that is a little bit smaller than that one. It is easy to see that both are larger than the recommended diameter.

Reducing the diameter of these beams will reduce the facial dose by approximately 80 percent and the gonadal, or scattered dose, by approximately 70 percent. Increasing total filtration will further decrease the facial dose by 55 percent and the gonadal dose to the patient and the operator's dose by approximately 30 percent. This reduction does not affect the diagnostic quality of the film.

Dental X-ray units which do not meet the recommendations of the Academy of Oral Roentgenology can be easily corrected by unscrewing the cone—all, I am sure, are familiar with the cone on the dentist's X-ray apparatus—and placing a lead washer in the aperture and adding aluminum disks—a washer of that type, for example, which can bring the beam size down to this small recommended beam of 2¾ inches. If we add aluminum of about 2 millimeters thickness, we can filter out the unnecessary X-rays in the form of the soft X-rays, which do not contribute much to the diagnostic quality. It contributes very little. These things cost only a few cents, I might add.

Our Rockville Laboratory notifies the State health department of our finding. It in turn notifies the dentist. In most cases the State supplies, without cost, the lead washers and aluminum filters. The great majority of dentists will immediately make the necessary corrections when this type of assistance is given.

I believe, Mr. Chairman and members of the committee, that this illustrates one of the things we are doing and illustrates also the way that unnecessary radiation exposure from X-ray can be reduced.

UNSAFE X-RAY EQUIPMENT

Mr. Fogarty. There are a great many X-ray machines in use, aren't there?

Dr. WEBER. Yes, sir, that is correct; about 170,000 in the United States at this time—about 90,000 of which are dental.

Mr. FOGARTY. Whey couldn't you get the manufacturers of these machines to agree to go to all of the dentists where they have sold the apparatus and make this change?

Dr. WEBER. Yes, I believe this is one of the approaches. As a matter of fact, we have plans for meeting with the manufacturers as our techniques are developed through our research and control and demonstration work. In addition to working with the manufacturers, of course, we must also work with the dentists and with the technicians.

Mr. FOGARTY. If it is as dangerous as you say it is, why shouldn't we make it public that this type of machine is dangerous and advise people not to be X-rayed, or else seize the machines?

Dr. WEBER. The latter, Mr. Chairman, of course would require legislative action, basic comprehensive authority.

Mr. FOGARTY. The Food and Drug Administration couldn't do it, could they?

Dr. WEBER. No, sir, I don't believe that the Food and Drug Administration could go into a dentist's office and have him discontinue the use of that machinery.

Mr. FOGARTY. What is the usual charge for an X-ray?

Dr. WEBER. The usual charge?

Mr. FOGARTY. The average.

Dr. WEBER. It depends on the type of X-ray, of course.

Mr. FOGARTY. That is why I changed it to "average charge."

Dr. WEBER. This would range all the way—and I must say, Mr. Chairman, I would have to submit to you the precise figures, but I can make an estimate, I believe. I would say the average radiograph of the chest probably costs about $5 to $10 per film.

Mr. FOGARTY. I am talking about the dental X-ray.

Dr. WEBER. I don't have information on what bill the dentist submits for an X-ray procedure. I think this is a program that can be effected without the vigorous prosecution of laws and without rules and regulations demanding it.

The professions are very cooperative on a purely professional basis.

Mr. FOGARTY. We shouldn't have one defective machine in operation today from the information you have given us.

Dr. WEBER. These are not just a few machines.

Mr. FOGARTY. I get impatient to get this information out once you get it. What have you done about it?

Dr. WEBER. It is being publicized. We are working on the program now with about 15 States. It is a very simple thing to do. All the dentist needs to know is how he can cut his beam down. This is the thing that does it. The big problem in any X-ray machine, in fact, is in the collimation—in the size of the beam.

That is easily correctible.

Mr. ACKERMAN. This is one of the reasons why we are asking for an increase this year—to push the program known as the program to minimize radiation in the healing arts.

Mr. FOGARTY. How much?

Mr. ACKERMAN. Our base is $405,000. We are asking for an increase of seven positions and $96,200.

BUDGET

Mr. Fogarty. Doctor, you are asking for $9,147,000, an increase of $1,487,000.

Dr. Weber. Yes, sir.

AGENCY ASSIGNMENTS OF RADIOLOGICAL ACTIVITIES

Mr. Fogarty. Will you first tell us what your activities in this field are limited to, and how they are different from the activities of AEC and the Food and Drug Administration.

Dr. Weber. I think I can put it this way: The AEC has primary responsibility under its act for not only the promotion of nuclear power, as you know, but also in connection with the regulating of hazards at the installations in the same way that any good industry would regulate its occupational health hazards that Dr. Magnuson talked about earlier.

The Public Health Service, while it has an interest in that—and I can describe later just how we are interested and what we do about it—is interested in the dispersal of any radiation out into the general environment that may result from the operation of those sources. In other words, as this might get into air, as this might get into water, as it might get into milk, as it might get into food.

Mr. Fogarty. Doctor, Atomic Energy justifies part of its budget on the work they do in "the evaluation of the significance of human exposure to radioactivity from all sources." It is given special emphasis.

Dr. Weber. I would say under their authority they would have a mandate to get into that field in order to protect their own people who are engaged in the management of these sources.

Mr. Fogarty. It was my idea that most of this type of work would be done by the Public Health Service; their load would be going down and yours would be going up. But the AEC is going up and up every year.

They also have a training program to go along with it, and so do you.

Dr. Weber. Yes, sir.

Mr. Fogarty. Is that training their people in their own shop like any other big industry would do?

Dr. Weber. As I understand it, that is the principal purpose of the training program—to prepare scientific personnel for work in AEC types of activities. For example, there would be considerable emphasis on nuclear engineers, for one thing; and also to a certain degree for health physicists. So I would say that their program is closely related to what I mentioned earlier.

They have responsibility for the proper management of sources.

Mr. Fogarty. For the plant.

Dr. Weber. Yes, sir.

Mr. Fogarty. What about the Food and Drug Administration?

Dr. Weber. The Food and Drug Administration, of course, also has its own act. This act requires them to look for all types of noxious agents in food, drugs, and cosmetics for the purpose of preventing the movement of material exceeding recommended standards in interstate commerce. When this is found, they can make cases under their law and proceed to prosecute.

In other words, it is close to being a legal function.

RESEARCH GRANTS

Mr. **Fogarty.** You are asking for an increase of $280,000 for research grants. Tell us in general the type of research and who does it and the results you receive.

VALUE OF RESEARCH GRANTS

Dr. **Weber.** First I might add, Mr. Chairman, these extramural grants have been transferred to us from the Institutes this year so we have had comparatively little experience with them as yet—just a few months' experience. We do, however, know what has been done in that program, since before the transfer an officer of our Division was an observer in the Radiation Studies Section. Therefore we know just what work they did.

First of all, as to who does it, these are in almost all cases—in the case of radiation—university staffs. No. 2, the type of project on which they work is the type of project which represents, I might say, the thing that the university is best able to do. They are in a little better position to do it than we are, and I will give an example here. One of the research projects is for the qualitative determination of whole-body dose to infants in a pediatrics department.

In other words, our Division does not have a pediatrics service. The particular university in this case has a pediatrics service, of course, and there are certain peculiarities with regard to radiation to whole body or parts of the body.

Infants would represent one of those special problems, since I think it is quite obvious it would be a little more difficult to confine the beam to a localized area in an infant than it would using the same device in an adult. For example, if my mouth were X-rayed, by sticking to a beam 2¾ inches in diameter, the dentist—if he has his X-ray machine properly focused—could take a picture of the tooth that he wanted to, and there would be very little scatter to the gonads.

By doing this in the infant—which is difficult to confine in the first place—with its small body compared to the adult you can radiate the eye; you can radiate the thyroid, and so forth.

Therefore I think the university is the best place to do that type of thing.

No. 3 is the fact that this university research really integrates with and supplements ours because it is a nondirected type of research. In the nondirected type of research, as we conceive of it, while the field may be radiation and is justified as in the field of radiation, the investigator is more free to explore the implications of radiation or other factors that may be implicated in it than we are, in that we usually apply our research efforts to the immediate practical problem.

Qualitatively, the research workers do not vary in that all are trained scientists, whether they are working on nondirected research or directed research of our type. So the chief product of that type of an arrangement—I am referring to reason three—is that we are able to get more new ideas as to how to attack things in the field—in other words, open up new avenues of exploration and at the same time also possibly correcting some of our own notions or own opinions on radiation matters.

In addition to that, the projects also reflect the fact that many scientific disciplines that we don't ordinarily use or do not use in any large number are in universities and they are turning their talents to radiation problems. I can cite, for example, clinical radiologists—of which we have some. I can cite geologists—of which we have none. I can cite other professionals who would be studying such things as the differential effects of radiation compared with other agents on a variety of animals or organs within animals—perhaps, for example, the recovery rate of mouse tissues to certain radiation dosages.

So I believe it is a very worthwhile program. It is integrated at the national level.

Mr. Fogarty. Would you put into the record, by Institute, the amounts NIH has transferred to you.

Dr. Weber. Yes, sir.

(The information requested follows:)

Radiological health—1961 comparative transfers from National Institutes of Health in 1962 estimates for research grants and review and approval of grants

From—	*Amount*
General research and services, National Institutes of Health	$443,000
National Cancer Institute	145,000
National Heart Institute	34,000
National Institute of Dental Research	34,000
Arthritis and metabolic disease activities	264,000
Neurology and blindness activities	21,000
Total transfers, 1961	941,000

FEDERAL SUPERVISION OF THE GRANTS

Mr. Fogarty. On page 179 of your justifications you refer to—

> grants for nondirected projects of their own design. In accord with established practice, investigators supported by grants will conduct research free from governmental direction and intramural program considerations. * * *

Since when has this been the established practice?

Dr. Weber. I don't know, Mr. Chairman; but I think it is a general question that Dr. Anderson or Dr. Terry could answer.

Dr. Anderson. This is the practice with regard to the research grants which are made to outside institutions in the pursuit of their research on specific projects. For example, you might direct us to do research relating to the control of X-ray exposures on the healing arts in our direct appropriations.

On the other hand, in the research grants program, the investigator who submits an application for his research project may not choose to work on this particular problem himself, but may choose some other aspect of radiologic investigation with regard, say, to the effects of dental radiation exposure upon the thyroid gland or upon the thymus gland in infants.

He might do this on his own; whereas we would be directed to studies of means for cutting down radiation exposure. This is the practice, though, with regard to all research grants provided by the Public Health Service—that the research investigator is free to submit his idea to a board of qualified reviewers who make a report upon the scientific and technical merits of his proposal and then it is funded by the specific appropriation which has a general program interest in this area, whether it be cancer or radiological health.

Mr. Fogarty. How do you know whether the grantee, after he gets the money, decides he wants to do something on heart research instead of radiological health? If you do find he has changed to a new field, what do you do about it?

Dr. Terry. Mr. Chairman, may I speak in this direction?

Mr. Fogarty. Yes.

Dr. Terry. It is true that in our project grants the person who makes the proposal is the one who determines the area in which he would like to work. He makes the proposal that he would like to do certain research in a particular area.

To state it as flatly as it is stated here is not quite correct because obviously our review bodies must take into consideration not only the technical ability of this man to do this, but the importance of his proposal to the overall program. Actually our grants are, in turn, related in part to our intramural program because we feel that, for instance, in a particular area like heart disease, if we are not working on an important problem in the field of heart disease in our own intramural research it becomes even more important that we support projects in this area by grants.

So they are not independent by any means. I think what was meant here by "in terms of governmental direction" was the question of the fact that we don't direct the person as to exactly what he should do.

One of the things that has been held very, very important to research workers in this country working with grant support is that if they encounter a lead during a proposed research project, and they feel that this lead is important to pursue, it is well understood within our policy framework that they are allowed to depart from their original proposal and to follow this lead, which I think is very important from the standpoint of giving a recognized investigator the opportunity to follow the leads that he wants to follow and the thing that he feels is most important at that time—because in outlining a program, even for a year in advance, one cannot always predict exactly what he will do because something else may turn up along in his investigation which leads him to believe that this is much more important, this thing which has come up possibly incidentally, to pursue.

So the general attitude is that our review bodies look at it from the standpoint of the technical competence and the feasibility of the proposal. Then further taken into consideration is the question of how important is this to our overall problem.

Then the grant is made on that basis. But if the investigator feels that something comes up during the period of this investigation which is more important for him to pursue, he may do it.

Mr. Fogarty. That is a little better explanation, I think, than you have in your justifications.

TRAINING GRANTS

You have $500,000 for training grants, which is no increase.

Dr. Weber. No, sir.

Mr. Fogarty. I think training is one of the areas where you ought to be spending more money.

Did you ask for any more money at the initial stage?

Dr. Weber. Yes, sir. We asked for $2 million for training grants next year.

Mr. Fogarty. And you ended up with $500,000?

Dr. Weber. Yes, sir.

Mr. Fogarty. That is a pretty sizable cut, isn't it? Will you supply for the record what you would do with that $2 million if it was appropriated.

(The information requested follows:)

Availability of the $2 million originally requested for training grants to universities and other educational institutions for the training of radiation health specialists, would permit us to support such training at a level recommended by the National Advisory Committee on Radiation in its report to the Surgeon General in March 1959. These grants are used to strengthen the number and variety of courses in the radiological health field and to develop new curricula designed to train radiation health specialists. This is done by using grant funds for procuring necessary specialized staff and equipment, as well as providing stipends for students desiring to become radiation health specialists.

Experience thus far during 1961 demonstrates that $2 million could be effectively used by the institutions requesting funds.

INCREASE FOR DIRECT OPERATIONS

Mr. Fogarty. You are asking for $7,449,000, an increase of $1,207,000, for direct operations. Will you explain that, please?

Dr. Weber. Yes, sir. First let us consider research. I should preface this, Mr. Chairman, by stating that we have been given the national responsibility for collecting data, analyzing, and assessing all sources of radiation exposure, and therefore, our program has been influenced by that assignment. This monthly report entitled "Radiological Health Data" indicates that. To begin with the research area, where a total increase of about $700,000 is asked, we would study a number of things—all tying into radiation exposure and assessment, which means evaluating the effects of this exposure; and the ways we would reduce exposure.

We have a projected increase of $700,000 designed to include such items as the interrelationship of environmental levels and body burdens. In other words, as materials come from the environment into the body, some of them are stored. Some of the projects under this are: The Animas River project—which I mentioned in my opening statement; the St. Louis project which extends from Missouri into Illinois, investigating factors contributing to radiation levels in the St. Louis milkshed—where some milk samples are high in strontium 90; and, in collaboration with Dr. Magnuson, to conduct study and research into effects of radiation exposure in uranium miners.

We also get into problems of radioactive waste disposal in various parts of the Northeast and Southeast particularly.

WASTE DISPOSAL IN THE NORTHEAST

Mr. **Fogarty.** What are you doing in the Northeast on waste disposal?

Dr. **Weber.** We have worked up there primarily with measuring radiation levels in the environment in the Portsmouth area—the site of the nuclear submarine construction; and, coming down a little bit, we also work on the Delaware River in monitoring the water there because this is the site of numerous industries and also the construction of the nuclear ship *Savannah.*

LEUKEMIA AND BONE SARCOMA

Mr. **Fogarty.** Do you find leukemia more prevalent in these areas than other areas of the country? There seem to be more cases of leukemia being reported every year.

Dr. **Weber.** There have been reported increases. I can't say that increases are due to ionizing radiation, however—in this particular case. The studies have not progressed to the area where you can ascribe that cause and effect. There are some peculiar situations in leukemia.

Mr. **Fogarty.** What about bone sarcoma? That seems to be on the increase, too.

Dr. **Weber.** Some have reported an apparent increase.

Mr. **Fogarty.** Have you heard that in any of the hospitals in Boston?

Dr. **Weber.** We have not attempted to analyze it. One of the things that would have to be disproved, before one could truly say that there has been an increase is that the diagnoses and the reporting of bone sarcoma are inaccurate. Bone sarcoma is not too common a disease. We usually discover it by metastasis to the lungs as a rule.

Mr. **Fogarty.** How can you tell whether there is an increase in the incidence of this kind of disease or whether we are using better methods of diagnosis?

Dr. **Weber.** I think the only way you can tell that, Mr. Chairman, is to follow the procedures which we are following and are recommending ourselves, namely, by the conduct of good epidemiology studies on population groups. As you know, in the science of epidemiology, our goal is to elucidate the complete pattern of a disease as it occurs in the population.

Take your first example, leukemia. We need to take into account all sorts of factors: Age, geographic distribution, types of treatment, drugs, what the environment happens to be like in terms of radioactivity or other agents; and then isolate that factor which may be responsible for a particular area being higher than another area, which does not have that factor.

I think you would have to do the same thing with bone sarcoma. Would you like me to proceed on research?

Mr. **Fogarty.** Yes.

METHODOLOGY AND INSTRUMENTATION

Dr. **Weber.** The next major heading is "Methodology and instrumentation." For the simple reason that in this particular field we rely almost entirely on instruments—even the microscope isn't too helpful to us in most of our work because we are dealing with agents at the submicroscropic level.

The third area is in biomedical effects. The fourth area of research is in data analysis and interpretation. The fifth area of research is to explore in greater detail radiation exposure from medical sources.

One of the main projects under this latter area is the investigation of the effects of iodine 131, which I mentioned in my summary statement, on patients who have received that agent. There apparently have been a number of cases of leukemia induced as a result of iodine 131 use and also some thyroid cancer. This reflects the fact that it is an unstable radioactive isotope of stable iodine. Iodine is a thyroid gland seeker. This is another one of our complicated problems. We have to remember the chemistry at the same time that we measure the dosage. This substantance seeks the thyroid. It is highly valuable, I might add, in medical diagnosis and in therapy. It has practically replaced, I think, the usual calorimetry to measure the BMR—basic metabolism rate—these days.

This very expensive elaborate BMR test is being replaced pretty much by iodine 131 administration. It is a very important radioisotope to study because some prominent radiologists have told me that within a period of 10 years the uses of radioisotopes in medicine will be competing with the diagnostic X-ray on terms of parity.

If you have some idea of how often our chest is X-rayed in routine physicals and other X-rays, I think you can see why we need to study the uses, the potential hazards, of some of these agents. By studies of this type, we will be able to determine reasonably safe use of these useful agents probably in reduced dosage under certain precautions.

Mr. Fogarty. What is meant by the term "atomic cocktail"?

Dr. Weber. I believe you are referring here to some of these radionucleides that are ingested for the purpose of visualization studies. Iodine 131 is often given in the form of a so-called atomic cocktail. In other words, if one drinks the solution containing it, the substance is absorbed; and, as I said, it seeks the thyroid. So this is something of very important practical application.

Then the radiation intelligence network is the next item under research, where we would seek to introduce the necessary refinements to know where we are in terms of population exposure.

STATE PROGRAMS

In the development of State programs, which is next, we are asking for an increase of $303,000. This provides no increase for the development of State programs themselves in terms of technical assistance. This is the assistance for States and regional offices including personnel assignments and also certain laboratory services.

RADIATION FROM MEDICAL SOURCES

The next is the program to minimize radiation in the healing arts. We are asking for $96,200, which is primarily for an expansion of this dental X-ray program which is in operation. It permits comparatively little expansion in the medical X-ray work.

SERVICES TO THE STATES

The next part of technical assistance is special technical and laboratory services to the States. Here again this is to increase certain technical facilities for work which would be carried out mainly through our own laboratories that I have mentioned. We now operate at four laboratories: One in Montgomery County, Md.; one at Las Vegas, Nev.; one at Montgomery, Ala.; and the fourth, of course, at Cincinnati, where we have operated for a number of years.

TRAINING

In the training area, we propose to increase that by $204,100, divided as follows: $46,000 increase for advanced training, which means increasing the number of officers that we detail for extramural training; an increase of $61,000 for specialized short-course training, a program which continues to be oversubscribed. This year we are training about 1,000 in short courses as compared to something like 600 last year, and we still have a backlog; $97,100 is for the development of training materials. So that summarizes direct operations, to which I believe the question was addressed, Mr. Chairman.

NEW YORK STUDY ON RADIATION AND CONGENITAL MALFORMATION

Mr. Fogarty. What results have you gotten from your New York study of certain radiological activities from rock outcroppings?

Dr. Weber. The results there, Mr. Chairman, have been in the form of organizing several States, including New York State, to carry out the epidemiological studies that are necessary and which I discussed a little bit earlier in broad terms.

As you know, that study was tied into the apparent appearance of a greater number of congenital malformations in the families of people living in high-background level areas as compared to those who were living in a lower background. So our first problem there was to find out just how we would attack this thing, because at the present time in the United States there are, I think, about 160,000 grossly visible congenital malformations reported each year. The true number is probably higher.

The first thing we have to investigate is the problem of diagnosis; namely, what physicians are calling congenital malformations. So we have begun to do that through certain assignments.

No. 2, we are carrying out more perfected measurements of the background. For example, in New York State, working with the State health department there, we have been cooperatively developing certain new background study techniques. One that has already been developed by them is a new, rather inexpensive, plastic gamma scintillator which picks up differences in background from one part of New York State to another.

In addition to New York State, if you would like the information, there are some other States now cooperating.

Mr. Fogarty. You can supply that for the record.

Dr. Weber. Yes, sir; I will be glad to.

(The material requested follows:)

In addition to New York, States presently participating in this work include Minnesota, Colorado, and Michigan. Another aspect of this work also is being conducted in a cooperative project with Johns Hopkins University to define standards for the clinical diagnosis and classification of congenital malformations.

REPORT OF THE NATIONAL ADVISORY COMMITTEE

Mr. **Fogarty.** Last year in the hearings we placed in the record the report of the National Advisory Committee on Radiation which made, we thought, some very strong recommendations as to the need for radiological health facilities in this country.

This committee of experts laid out a program that would cost $50 million to be reached in 5 years. Is this budget heading toward that program?

Dr. **Weber.** I would say, Mr. Chairman, in view of the increase that it is a step in that direction.

Mr. **Fogarty.** It is a pretty short step, isn't it? They suggested $50 million in a 5-year period. So, where are you?

Dr. **Weber.** As I recall, in the summary, the report recommended that the program start out gradually and for the fiscal year 1960 there be an appropriation of $2.5 million—which we did get from the Congress, about $2.6 or $2.7 million, something like that— and then progressively increase until the $50 million is reached.

We are now approaching the third year of operation under this recommendation in this particular budget.

Mr. **Fogarty.** In 1962, what should we be appropriating to keep pace with their recommendations?

Dr. **Weber.** That is a difficult question. I might defer to some of the discussions that have gone on within the Department.

Mr. **Fogarty.** I am not concerned about those discussions. What should we be appropriating this year to keep pace with this $50 million budget?

Dr. **Weber.** I believe this sum was indicated in the figure that we originally requested for this fiscal year.

Mr. **Fogarty.** How much was that?

Mr. **Ackerman.** $15,246,000.

Mr. **Fogarty.** As compared to what?

Mr. **Ackerman.** $9,147,000.

Mr. **Fogarty.** So that means we are about $6 million behind the recommendations of this Advisory Committee.

Dr. **Weber.** Yes, sir.

Mr. **Ackerman.** Yes. The reason I hesitated is that, there are complications in comparing that precise figure. The $50 million figure included a grant support for States item. But I do believe the Division, in framing its budget here which does not include special support to States, shooting at keeping up to the schedule of this recommendation of the National Advisory Committee on Radiation.

Mr. **Fogarty.** If you receive all you requested, would you be in line with their recommendations?

Dr. **Weber.** Fairly close to it because, as Mr. Ackerman has indicated, our earlier 1962 estimate did not take into account the category of grants to States, although the estimate did include research grants.

I might add that the NACOR $50 million goal did take into account financial assistance to States and research contracts. So I would say that with the States item added to the original 1962 estimate it would be geared in with NACOR's recommendations.

Mr. FOGARTY. If you wish to refine this for the record you may do so.

(Dr. Weber provided the following for the record:)

The NACOR recommendation was as follows:

"It is anticipated that the cost of a comprehensive program of radiation control which includes the elements set forth in the foregoing recommendations will reach a level of approximately $50 million in a period of 5 years. The committee recommends, however, that the program be developed gradually, perhaps at a level of approximately $2,500,000 in the fiscal year 1959–60, and increasing in magnitude until full development is reached in 1965. Even with such progressive staging, the committee recognizes that the program is a substantial one. However, the criterion of realistic need has been continually before the committee in its deliberations. There is no question that the present situation calls for bold and decisive action. With such action based upon sound principle, the committee believes that the Federal Government should proceed with all deliberate speed."

Our original request for 1962 was in accord with the schedule recommended by the committee and called for a program level of $15 million. A detailed break of this amount has been furnished in reply to another question.

LEGISLATION FOR RADIOLOGICAL HEALTH

Mr. FOGARTY. Last year when we asked about your plans for support and stimulation of State programs we were told that consideration was being given to the question of a legislative proposal in the radiological health field. What have you done about it?

Dr. WEBER. Mr. Chairman, the question of legislative proposals is being developed, as I understand it, within the Department at this time. I don't know what will finally be developed. At any rate, we have been asked for our recommendations—let me put it that way. In other words, the notion is being entertained. I don't know whether it will go forward this year or next year, or whether it will be some time further in the future.

Mr. FOGARTY. Do you know, Mr. Kelly?

Mr. KELLY. I really don't.

Dr. TERRY. I think Dr. Anderson has some information on this, Mr. Chairman.

Dr. ANDERSON. The desirable features that we might look for in legislation are being discussed now within the Department. The outcome of these discussions has not been determined yet, Mr. Fogarty. But there is interest in this area in the Department.

Mr. FOGARTY. Have you made any progress since a year ago?

Dr. ANDERSON. Yes. There is still no bill which has come out from the Department; but there is active discussion and interest in this field in the Office of the Secretary.

Mr. FOGARTY. In what area? What are you thinking about?

Dr. ANDERSON. With regard to the whole field of radiological health, which is the protection of the population from radiation exposures, whether they be from medical X-rays or nuclear devices. We are discussing such things as the ways in which support for State programs might develop, categorical grants or something of that sort, and project grants.

We are discussing the control aspects with regard to the ways in which the Public Health Service might be effective with the States in limiting exposures.

LABORATORIES

Mr. Fogarty. You have four laboratories, but you don't have any in the northeastern section of the country.

Dr. Weber. No, sir.

Mr. Fogarty. Is there any good reason for that?

Mr. Denton. There isn't one in the Middle West, either.

Dr. Weber. In our long-range plan, Mr. Fogarty, we did include the northeast site as the next laboratory to be developed. It would be of the type the Las Vegas and Montgomery laboratories are now.

At the present time Montgomery does samples for 30 of the Eastern States; and Las Vegas does it for the 20 westernmost States. I might also note that part of the environmental health center plan which Dr. Anderson has described does contemplate the use of regional and special-purpose laboratories.

So I might say in this connection that in considering a northeastern laboratory, we have taken into account its relationship to the environmental health center planning and its role as a part of the whole in the national program.

Mr. Fogarty. Mr. Denton?

Mr. Denton. I have a building in my district which would be just the thing for a laboratory, if you are looking for one there. It was a quartermaster depot—a new building, a very fine building. The military abandoned the quartermaster depot and the Census took it over. Now the Census is through, and there is a great deal of unemployment there. It is a very fine building. If you are looking for a laboratory, I would recommend it to you very, very highly.

Dr. Weber. Thank you.

STRONTIUM 90 AND OTHER FISSION PRODUCTS

Mr. Denton. Is strontium 90 caused solely by an atomic bomb explosion?

Dr. Weber. It is a fission product. It would come from any type of nuclear fission reaction. Of course, nuclear fission reactions are best known through weapons explosions—atomic weapons—but strontium 90 is also produced in nuclear reactors.

Mr. Denton. Is it very dangerous?

Dr. Weber. Yes, sir. It is a very, very toxic radioactive element.

Mr. Denton. I have heard that it got in milk; it got on the grass and the cows ate it.

Dr. Weber. It is very highly toxic. Of course, the amount that has gotten into the environment now has been in the form of traces.

Mr. Denton. I understand the use of atomic power for the healing arts, but in industry it is not very widely used, is it?

Dr. Weber. Not as yet.

Mr. Denton. Even when it is used there is not much radiation from it: is there?

Dr. Weber. No, sir; that is because these are closed-circuit reactors.

Mr. Denton. I was on the *Nautilus*, and they had a geiger counter there. There was more radiation from my watch than there was right by that engine—I guess you would call it an engine.

Dr. WEBER. Yes, sir; that is true. That is because these devices are very heavily shielded. The weapon, on the other hand, of course is exploded for military purposes, in which case your objectives are radically different. So they will require substantially different control measures to protect against the fallout that we are seeing.

Mr. DENTON. What about the weapons?

Dr. WEBER. The weapons testing, of course, has been suspended, as you know.

Dr. DENTON. As far as the atomic bomb is concerned; yes.

Dr. WEBER. Yes; there have been no weapons exploded since 1958 by our country.

Mr. DENTON. We would know if anybody else did, wouldn't we, unless it was underground?

Dr. WEBER. Yes, sir. The French have exploded two in the Sahara, the Hiroshima-Nagasaki type, about 20 kilotons.

Dr. ANDERSON. Mr. Denton, if I may, on this point, Dr. Weber mentioned there is considerable experimentation with regard to the possible uses of the nuclear reaction produced power for propulsion of various devices, as well as for power for communications.

Each of these uses, if it develops fully, may contribute something to the potential hazard.

Mr. DENTON. You want to be ready for what is going to happen.

Dr. ANDERSON. We would like to be ready.

Mr. DENTON. I think that is very commendable.

Dr. ANDERSON. These new uses require some ingenuity on our part to adapt a control readiness, if you will, to the possible industrial application.

Dr. WEBER. I think at this point, if we could make one or two remarks off the record, it might help on this last program.

(Off the record.)

COOPERATION WITH AEC

Mr. DENTON. Just one last question. Again there seems to be somewhat of a conflict between you and Atomic Energy on this.

Dr. WEBER. In what respect, Mr. Denton?

Mr. DENTON. You are both doing research work on the effects of radiation.

Dr. WEBER. Yes, sir; we both are.

Mr. DENTON. It seems to me there is a duplication of effort there which someplace along the line should be eliminated.

Dr. ANDERSON. Possibly on this a few words on the Federal Radiation Council and the Executive order would be helpful.

Mr. FOGARTY. Either one of you may answer.

Dr. WEBER. Dr. Anderson has mentioned the Federal Radiation Council, which was set up a little over a year ago to develop standards of exposure in the field, and in which several agencies cooperate: namely, the Department of Health, Education, and Welfare: the Atomic Energy Commission; the Department of Defense; and the President's scientific adviser as exofficio, and the Department of Labor.

So we are together on the planning of standards. By the same token, we also plan the programs which are necessary to give us better standards—standards both of actual exposure permitted as well as performance standards; that is to say, techniques.

As an outgrowth of that, even preceding it, the Bureau of the Budget within the executive branch has made a study of the programs of each of our agencies. They have come up in their study with the conclusion that there is no duplication between the AEC grants on the one hand for certain purposes, and the Public Health Service work on the other.

The Executive order also spelled out the respective responsibilities of the various Federal agencies that I have named. In our case, as I have said earlier, we were given the responsibility for estimating exposure from all sources, as well as assessing it. The assessment means we must do research to discern the effects of these exposures—exposures either partially or in toto.

So therefore we follow these broad principles and justify our activities in these terms. In other words, if we find that there are gaps in knowledge which need to be plugged by research, so to speak, which are keeping us from setting up acceptable standards, these are the areas that we hit strongly and largely through this epidemiological approach which I mentioned. So the approach is quite different from the AEC or DOD.

Mr. Kelly. To carry this out, too, Mr. Denton, we exchange our detailed justifications between AEC and the Public Health Service, and between the Public Health Service and Food and Drug Administration, to be sure we have coordinated programs.

Mr. Denton. That is all.

Mr. Fogarty. Mr. Michel?

COOPERATION WITH THE DEPARTMENT OF AGRICULTURE

Mr. Michel. Doctor, is there any correlation or exchange of information with the research activities of the Department of Agriculture, particularly with respect to strontium 90?

Dr. Weber. Yes, sir. We work closely with them. They are one of the contributors to our radiological health data and help to prepare it each month. That is No. 1 and this concerns sources.

Then I would like to cite an example of a specific project in which we cooperate with them, namely, the project seeking practical methods to diminish the strontium 90 content of milk. So we work with the Department of Agriculture and the AEC and have set up a tripartite laboratory out here in Beltsville.

Mr. Michel. I am sure in the hearings last year Dr. Clarkson mentioned this item. Then your having brought it up here today makes me wonder whether or not AEC, Agriculture, and the Public Health Service are really cooperating rather than competing.

Dr. Weber. Yes, sir. That is even progressing past the point that you mentioned last year. For example, the Department of Agriculture is giving us some very valuable information on national diets, dietary intake, dietary habits, and so forth. This illustrates how the strength of one department in carrying out its legal responsibility can contribute to the work of another. In this case ours, because this data relates to our interest in, and measurement of, the samples we are collecting of air, water, food and milk—in various parts of the United States.

In order to find out just what we call the integrated doses in an individual, whether it be you or I or anyone else, from a multitude of sources, with this multitude of sources being one of the reasons that it makes this field quite a confusing business, we have to take into account in what form these things are taken in; as well as food preferences of various age groups, and so forth.

For example, you may remember about a year ago the Secretary had to get out a special press release on high strontium 90 in bran. This was very high. Very rapidly we were able to get information from Agriculture and from other sources as to what the probable consumption of bran was by the average American.

When we found out what that figure was, it became quite apparent that bran as a source of intake, despite the fact that on a unit basis—in this case, micro-micro curies per kilogram—its radiation content might be relatively high, was a very negligible contributor of strontium 90 because of the food habits of the American people and the type of bran it was.

So I think this illustrates right here that we do take advantage of the strength of other departments and do this consistently. Of course, one needs to do this because the radiation field actually relates to all departments of Government. We could never conceivably take care of all of it. We are merely a focal point concerned with the health and safety aspects of the population of the United States as a whole. That is in keeping with the Surgeon General's responsibility under section 301 of the Public Health Act.

DENTAL X-RAY EQUIPMENT

Mr. Michel. Getting back to the discussion of dentists and the use of X-ray, I wasn't aware of the problem that we discussed here today before now. Did I understand you to say there has been good cooperation from the dentists around the country? There was something during the course of your testimony that leads me to believe that there is no compulsion on the part of a dentist to comply and to make these corrections or modifications that should, sometimes, be made.

Dr. Weber. I am sure I gave that impression because, in fact, I had to limit my remarks to certain aspects. To take up your questions in order, No. 1—and this is without any attempt whatsoever to make some of my friends in the American Dental Association feel good—the dentists have been outstanding in their cooperation.

Before our Division got into operation in 1958, I believe the dentists in Connecticut voluntarily developed their own program for the reduction of exposure although it wasn't this particular technique, because this technique wasn't available.

Mr. Michel. Does this come about in any make of machine?

Dr. Weber. Yes, sir. This can be done on any machine. The manufacture of machines is pretty good as they are turned out from the factory. We don't really have to worry about that. It comes in the use.

The machine gets bumped, handled, shipped, and so forth. You often have difficulty getting repairs on them. The New York City Health Department ran into a case, I believe it was on a fluoroscope in New York City, where the screen was broken and somebody—instead of replacing it with lead glass—put in ordinary window glass.

So you get all these types of things. In other words, what we really are arguing for here is to strengthen the Federal-State-local official health complex with competencies in this field so these people can go in and help with the physical checks of equipment, because all that we are doing here really is carrying out the role of the official health agency looking into the mechanical details of the X-ray usage.

We do not believe we should tell a dentist or a physician when he shall make an X-ray examination. This is a professional decision. We couldn't practice modern medicine without the X-ray; there is no question about that.

However, we do want to be in a position where we can help the physician and the dentist to make certain that he is operating with safe equipment. This is our real motive here.

Therefore I would say you might want legislation requiring registration of sources so we know where the X-ray machines are so as to be better able to give consultation. I would not push at this time for legislation which would, specifically spell out the authority to go in and put an X-ray machine out of business. As we get experience with this work, we might have to get into that stage sometime later.

Mr. Michel. Would you recommend that the States themselves take that kind of action?

Dr. Weber. Really that is the way we are doing it.

Mr. Michel. We have our own State and local inspection services for weights and measures in butcher shops and feed stores to see if they are giving their customers proper measurement and for many other things. It would seem to me that it would be very much in order if every dentist's machine came under inspection as automobiles, scales and other things have to.

Dr. Weber. Your State is one of those that requires registration of sources.

Mr. Michel. I am glad to hear it. How many States, incidentally, require this?

Dr. Weber. I would have to look up the exact figures.

Mr. Michel. Would you furnish that for the record.

Dr. Weber. Yes, sir.

(The information requested follows:)

Twenty-six States require registration of X-ray machines (as of October 20, 1960).

Dr. Weber. We have been working with the Council of State Governments on the development and also the adoption of uniform model laws for the control of radiation hazards. We have to await the results of the present legislatures this year to see how many States did pass that legislation. I think it will probably come up to about a dozen or more.

HISTORY OF BUDGET REQUEST

Mr. Fogarty. Before we go on to the next item, will you place in the record the complete history of your 1962 budget request.

(The requested information follows:)

Radiological health reductions made between preliminary estimate and Bureau of Budget allowance

	Request to Department (1)	Request to BOB (2)	BOB Allowance (3)	Difference between cols. 3 and 1 (4)
1. Research:				
(*a*) Interrelationship of environmental levels and body burdens	$1,138,000	$1,117,900	$827,300	−$310,700
(*b*) Methodology and instrumentation	1,046,600	698,500	656,200	−390,400
(*c*) Biomedical effects	1,240,000	1,045,600	950,100	−289,900
(*d*) Data analysis and interpretation	258,400	171,400	166,900	−91,500
(*e*) Radiation exposure from medical sources	439,000	202,000	199,200	−239,800
(*f*) Radiological intelligence network	1,593,000	802,000	561,000	−1,032,000
Total research	5,715,000	4,037,400	3,360,700	−2,354,300
2. Technical assistance	4,992,900	3,274,200	2,885,200	−2,107,700
3. Training	1,340,100	1,204,400	1,203,100	−137,000
Total direct operations	12,048,000	8,516,000	7,449,000	−4,599,000
4. Research grants	1,198,000	1,198,000	1,198,000	
5. Training grants	2,000,000	2,000,000	500,000	−1,500,000
Total request	15,246,000	11,714,000	9,147,000	−6,099,000

Mr. FOGARTY. Thank you very much. We will reconvene at 1:30.

AFTERNOON SESSION

BUDGET AMENDMENTS, 1962

Mr. FOGARTY. The committee will come to order.

Mr. Kelly, do you think there are any other revised budgets coming up for this Department?

Mr. KELLY. There are two items under consideration that have not been resolved yet, one related to the Environmental Health Center and the one related to the Office of Education, with particular reference to research. And the other relates to new legislation, aid to dependent children——

Mr. FOGARTY. What about the Institutes of Health, is there another budget amendment being considered on that?

Mr. KELLY. That has been decided.

Mr. FOGARTY. Are you sure?

Mr. KELLY. Yes.

Mr. FOGARTY. As far as the executive branch is concerned, you are not sure about what Congress is going to do?

Mr. KELLY. No.

Mr. FOGARTY. You have a pretty good idea, though, don't you, from past experience?

WATER SUPPLY AND POLLUTION CONTROL AND GRANTS FOR WASTE TREATMENT WORKS CONSTRUCTION

Well, we had better go ahead with water supply and pollution control. Mr. McCallum, are you going to give us a statement?

GENERAL STATEMENTS

Mr. McCallum. Mr. Chairman, and members of the committee, I have been designated to testify on the appropriations for waste treatment works construction, as well as water supply and pollution control.

Mr. Fogarty. Are you going to take both?

Mr. McCallum. Yes, sir.

I should like to submit a statement for each program for the record, and summarize them orally.

Mr. Fogarty. That will be all right.

(The statements referred to follow:)

Water Supply and Pollution Control

Mr. Chairman and members of the committee, the Federal Water Pollution Control Act of 1956 (Public Law 660) authorizes a broad base for a balanced national water pollution control program. This request will continue the orderly implementation of several programs authorized by the act.

The proposed increases provide a balance among programs which takes into account both immediate and long-term needs. This order of program developments reflects recommendations of the presidentially appointed Water Pollution Control Advisory Board, special consultants to the Public Health Service, State officials, and national organizations. Specifically, the increases will be primarily for—

(1) Expansion of the project to develop a comprehensive water pollution control program for the Great Lakes-Illinois Waterway drainage basins;

(2) Enforcement proceedings and factfinding investigations, including the St. Joseph, Mo., court case and the Colorado River Basin studies;

(3) Expansion of the interstate national water quality network; and

(4) Research in the physical-chemical separation of pollutants from water, aimed at developing entirely new, more effective waste treatment processes to reclaim used water for use again, including such high order needs as drinking.

The National Conference on Water Pollution, which met last December, was called by the Surgeon General pursuant to the request of President Eisenhower. In accordance with the President's proposal, the Conference provided a forum in which all interests concerned—industry, agriculture, health, conservation, and recreation, as well as State and local governments—could confront and better appreciate their mutual responsibilities. The recommendations of the Conference, like those of the Advisory Board, support the major program plans reflected in this budget.

The conference endorsed "* * * The positive policy of keeping waters as clean as possible, as opposed to the negative policy of attempting to use the full capacity of water for waste assimilation."

On this premise the Conference recommended adoption of the following credo:

"(*a*) Users of water do not have an inherent right to pollute:

"(*b*) Users of public waters have a responsibility for returning them as nearly clean as is technically possible; and

"(*c*) Prevention is just as important as control of pollution."

Among a number of more detailed recommendations for specific action the Conference stated:

"Planning for the comprehensive development of each major basin or water resource area should be established as a fixed national policy."

COMPREHENSIVE PROGRAMS FOR WATER POLLUTION CONTROL

A comprehensive program for pollution control provides for the orderly and efficient conservation of water quality in the development and use of waters in an entire drainage basin. It is based on cooperative study and agreement on water quality objectives by all Federal, State, and local agencies and industries concerned with water use in the basin. It requires determinations of present and future pollution, its causes, and its effects on present as well as future beneficial water uses. It outlines time schedules for the pollution control, and preventive measures that are necessary to achieve the desired protection and maintenance of water quality.

Comprehensive water pollution control programs will need to be developd for all major river basins. The order by which the Public Health Service initiates these projects is based on: (1) the needs of Federal agencies for the kinds of data developed in a comprehensive program; and (2) the water supply and pollution control needs of State and local agencies, and industry.

Two major comprehensive water pollution control programs now underway are receiving a great deal of attention at this time. The first of these is the Arkansas-Red River Basins project, started in 1957, and the second is the Great Lakes-Illinois Waterway Basins project, begun in 1961.

The Arkansas and Red Rivers, with their tributaries, are the major water resources of important parts of Kansas, Arkansas, Oklahoma, Texas, and Louisiana. The principal pollutants in these basins are mineral salts of both natural and man-made origin which seriously degrade water quality, preventing full population and economic development of the region.

The Arkansas-Red River Basins project is being carried out in cooperation with other Federal agencies and the State agencies, municipalities, and industries concerned. After 3½ years of field surveys and studies, it appears that feasible measures can be developed which will reclaim and protect an annual average of 25 million acre-feet of water—enough to supply four metropolitan New York cities. These measures, when carried out, will permit greater utilization of the region's water resources.

About half of the proposed increase for direct operations is assigned to the Great Lakes-Illinois Waterway Basins project. The initial phases of studies will be directed toward meeting the requirements of the Department of Justice, which has requested assistance in the complex and precedent-making litigation involving diversion of water from Lake Michigan.

The Great Lakes-Illinois Waterway project is the largest of its kind yet undertaken, involving as it does the greatest impoundment of fresh water in the world, which serves a rapidly growing, highly populated and industrialized region. Pollution in the Great Lakes differs from that in streams because it accumulates and is not carried away.

ENFORCEMENT

In September 1960, the first court action brought under the Federal Water Pollution Control Act was filed by the Justice Department in a U.S. district court, against St. Joseph, Mo. This being the first case of its kind, there are no guides or precedents. This makes it necessary that the Public Health Service provide extensive data, evidentiary materials, exhibits, and expert witnesses.

A substantial part of the increase will be used to extend studies and investigations being made in the Colorado River Basin enforcement survey, begun late in fiscal year 1960 at the request of the States in the basin. This action will involve studies and investigations of the Colorado River and all of its 60 tributaries which drain one-twelfth of the land area of the continental United States. One of the sources of pollution is radioactive wastes from uranium processing mills that produce one-third of the Nation's output.

In order to make certain that the Government's own house is in order, in 1960 the President requested the Secretary of Health, Education, and Welfare to take the lead in developing an inventory of the pollution situation at Federal installations. The Water Pollution Control Advisory Board has given much attention to this problem and recommended that all appropriate actions be taken to see that remedial measures are provided by Federal installations. It is expected that the inventory of pollution from these installations will be completed in fiscal year 1962 and will provide the basis for a case-by-case program to abate such pollution.

The increase for basic data activities in 1962 will be largely used in increasing the number of interstate stations in the national water quality network, and for providing the additional staff and laboratory facilities required to support this expansion and for giving assistance to State water quality basic data programs.

Reliable data on the quality of the Nation's waters are essential. The value of continuous data on our interstate waters is already being demonstrated by the analysis of that which has been compiled since the beginning of our national network in 1957. These limited observations are beginning to show the beneficial effects of pollution control in some cases, as well as to indicate deterioration of water quality in others. The value of the data increases with the number of sampling stations and the number of years for which they have been operated.

RESEARCH

Since 1940 water pollution problems have developed rapidly in number, magnitude, and complexity. Water pollution research has lagged far behind the growing needs with the result that there is inadequate intelligence available to cope with the many difficult problems urgently requiring solution.

The backlog of needed research continues to multiply as entirely new pollution problems are created by a rapidly growing population and industry which are concentrating in metropolitan centers, and by changing and complex industrial and agricultural technologies. These and other factors have resulted in substantial changes in the character and amounts of wastes being discharged directly to streams, and reaching them through land runoff. Present knowledge is largely based on problems of the past. Consequently, it is inadequate to deal with many of the newer situations confronting us.

Water pollution research requires a broad, intensive effort. This will demand many skills new to this field, such as physics, theoretical mathematics, and physical, colloidal, and other highly specialized branches of chemistry. Entirely new approaches to the problems will need to be developed.

The increase in research will be directed primarily to new methods of treating wastes which will remove a greater portion of impurities. Present treatment methods leave many dissolved contaminants virtually unaffected, including most of the new, synthetic chemicals, with the result that they are discharged to streams and find their way to downstream consumers. Now, in an increasing number of drainage basins, municipal, industrial, agricultural, and recreational activities must utilize waters that already have passed through upstream municipal and industrial water and waste systems, and overfertilized and pesticide-treated lands. As water is reused, the residual contaminants left by the inadequacies of present treatment methods build up. This includes the new pollutants which. singly or in combination, may have significant health effects. These treatment resistant substances are already causing problems downstream from a growing number of our cities.

The goal of this research project is to develop processes for treating municipal wastes that will approach the complete purification of waste waters. These processes will be based on new physical and chemical concepts for the separation of waste contaminants from water.

RESEARCH GRANTS

In concert with direct Federal operations in research is the work of the universities, which often have resources uniquely adapted to the study of particular kinds of problems. Research grants are beginning to bring to bear the efforts of this research potential on water pollution problems. The interest stimulated is indicated by the growing number of projects being supported and the applications being received. For example, at the end of fiscal year 1956 there were 41 research projects supported by grants in this field; at the end of 1960 there were 131 projects.

There is requested for this program for 1962 $15,028,000, an increase of $2,885,700 over the 1961 budget of which $606,000 is for research grants and $2,279,700 for direct operations.

Mr. Chairman, I shall be glad to answer any questions you may have about this program and the budget request.

Grants for Waste Treatment Works Construction

Mr. Chairman and members of the committee, the Federal Water Pollution Control Act of 1956 authorizes grants to cities and other specified jurisdictions for construction of necessary sewage and waste treatment works. The act authorizes $50 million per year, with the aggregate of all appropriations not to exceed $500 million. These are stimulatory grants, limited to 30 percent of project cost or $250,000. whichever is the smaller.

This grant program has provided significant stimulus to construction of essential waste treatment works. As of February 15, 1961, 2,600 grant offers have been made for projects certified by the States and meeting the other requirements of the act. These grant offers total $215 million, from aggregate appropriations of $232 million. The stimulatory effect of the grant is shown by the average ratio of 1 Federal grant dollar to approximately 5 local dollars in grant projects. The rate of construction of these municipal water pollution abatement works has averaged about $360 million per year compared to an average annual construction rate of $222 million for the 5-year period of 1952–56. Information supplied by the States indicates that there exists a backlog of about $2 billion in sewage treatment works construction requirements. This includes 5,200 sewage treatment plants and associated interceptor and outfall sewers.

It is estimated that the $50 million requested for fiscal year 1962 will provide grants for 570 projects.

Mr. Chairman, I shall be glad to answer any questions concerning this program and the budget request.

WATER SUPPLY AND POLLUTION CONTROL

Mr. McCallum. Congress, in enacting the Federal Water Pollution Control Act of 1956, made clear its intent that this national program is to conserve waters for all legitimate uses—public water supplies, aquatic and wildlife—recreational, agricultural, and industrial purposes.

The act provides for a cooperative approach among Federal, State, and local governments and industry. The job is twofold: First, to roll back excessive pollution that now exists, and second, to develop measures to avoid future pollution incident to population growth and technological change.

The appropriation request for 1962 continues implementation of the provisions of the act—on a reasonable and balanced basis.

More specifically, under immediate needs we propose to increase enforcement activities, extend the national water quality network, and strengthen technical assistance. Under long-range needs we propose to develop comprehensive programs to correct and prevent future pollution and to accelerate research to find answers to a growing list of problems.

Mr. Chairman, I know your committee is familiar with water pollution and with the urgency of corrective action. Water needs are increasing, and it is well established that water pollution control is a major factor in water conservation. We are quite encouraged by the growing public awareness of this situation, and the strong positions that have been taken by numerous national groups. For example, the American Water Works Association has undertaken a nationwide program pointing up the deficiencies in our water supplies and the need for positive action to abate pollution.

RECOMMENDATIONS OF WATER POLLUTION CONTROL CONFERENCES

The Water Pollution Control Federation, an organization of 10,000 experts in this field, issued a special statement on water pollution in its Philadelphia meeting last October.

I have a copy of that statement.

Mr. Fogarty. We will put that in the record.

(The statement referred to follows:)

[From the Journal, Water Pollution Control Federation (formerly Sewage and Industrial Wastes), November 1960]

Statement on Water Pollution Control

(Adopted by the Board of Control of the Water Pollution Control Federation, October 6, 1960)

Pollution of the Nation's watercourses, ground waters, and coastal waters is a continuing hazard to health, comfort, safety, and economic welfare. While considerable progress has been made in pollution control by many municipalities and industries, many water resources areas are being degraded, impaired, and damaged by such discharges, and they will be further adversely affected by the amount and pattern of population growth, industrial expansion, and technological advancements.

To assure the conservation and protection of the Nation's water resources, the Water Pollution Control Federation believes:

1. That the discharge of pollutional wastes into the waterways of the Nation should be controlled.
2. That the type and extent of treatment and control for any specific situation must be determined after consideration of the technical factors involved.
3. That the responsibilities for the adequate treatment and control of wastes to overcome pollution must be shared individually and jointly by industry and local, State, and Federal Governments.
4. That basic and applied research by competent personnel must be encouraged by broad mutual effort to develop new knowledge that will solve water pollution problems.
5. That the administration of pollution control must be firm, effective, and equitable.
6. That the administration of State and interstate pollution control programs should remain in the hands of State and interstate water pollution control agencies which must be supported by increased budgets and adequately staffed by well-trained and compensated engineers, scientists, and other personnel.
7. That the primary objective of pollution control is the protection of the public health, with other objectives adding impelling reasons for water resources protection.
8. That Federal activity in water pollution control should be administered by the Public Health Service, the organization best fitted to perform these functions by virtue of its long experience and close cooperation with State health departments and State and interstate water pollution control agencies.
9. That the public must be made fully aware of the hazards of pollution and of the workable means for control, so that it will sponsor and support construction and proper operation of all necessary facilities.
10. That mandatory certification or licensing of better-trained and compensated operating personnel is the best ultimate means for assuring the most effective operation and maintenance of pollution control facilities.
11. That standards for radiation hazards in water pollution control should be primarily in the interest of the protection of the public health.
12. That the control of toxic and exotic chemicals should be exercised, to the maximum extent practicable, at the source in order to prevent problems in water pollution control.
13. That Federal, State, and local fiscal laws and practices should be devised and modified to assure the most economical and effective means for financing the construction, operation, and upgrading of wastewater treatment works.

Mr. McCallum. Last year the Conference of State Sanitary Engineers spoke out forcefully on the pollution issue, urging increased research and continuation of an expanded construction grants program. Especially encouraging is that in addition to these professional groups, the conservation people and other large national organizations are actively supporting efforts to clean up our waters.

The General Federation of Women's Clubs has incorporated water pollution in its action program for the next 2 years. In launching this program, the Federation states:

> The necessity to control pollution of our water resources and the eventual elimination of pollution is no longer debatable—it is a must.

NATIONAL CONFERENCE ON WATER POLLUTION

All of these organizations were represented at the National Conference on Water Pollution held in Washington last December. Thirty recommendations came out of the conference. I mention this increased awareness because it indicates a deep and growing public concern over water pollution.

I have here a copy of the 30 recommendations of the national conference.

Mr. Fogarty. That will be put in the record.

(The document referred to follows:)

Recommendations of the National Conference on Water Pollution

1. That the conference express its conviction that the goal of pollution abatement is to protect and enhance the capacity of the water resource to serve the widest possible range of human needs, and that this goal can be approached only by accepting the positive policy of keeping waters as clean as possible, as opposed to the negative policy of attempting to use the full capacity of water for waste assimilation.

2. The adoption of a national credo, to be given as wide and consistent publicity as is feasible. The content of the credo would be: (*a*) users of water do not have an inherent right to pollute; (*b*) users of public waters have a responsibility for returning them as nearly clean as is technically possible; and (*c*) prevention is just as important as control of pollution.

3. There is need for a more systematic approach to the evaluation of the water pollution problems, to include health, esthetic, and market values. A framework for analysis must be developed which will provide a relatively precise understanding of benefit-cost and which will form the basis for the design of public policies and programs for effective water quality management.

4. Planning for the comprehensive development of each major basin or water resource area should be established as a fixed national policy. By comprehensive development we mean the application of integrated multiple-purpose design, planning, and management which include the joint consideration of ground and surface waters, systematic conservation by water users, and the treatment and management of waters having substandard quality. Consideration of every appropriate technique would be a routine part of planning for such development.

Such planning, insofar as feasible, should include consideration of all important industrial plant sites. An early and important objective should be a systematic program of flow regulation. State initiative toward comprehensive planning should be encouraged, and participation by all major interests should be encouraged. The objective should be one of eventually producing maximum total benefits from all economic and social uses.

5. Provision should be made, legally and financially, for the identification and acquisition at an early date of reservoir sites needed in the execution of comprehensive plans. The mounting population, the spread of settlement, and general intensification of valley land use otherwise may make many good sites totally unavailable or prohibitively costly.

6. The value of soil conservation, sediment control, and salinity control as pollution abatement measures should be recognized through planning and budget in our National, State, and local resource development programs. They should be considered as tools to be applied in water development and management. Pollution abatement is a problem with roots in rural land use and agronomy, as well as in urban congestion and industrial growth.

7. The public policy formally recognize the recreation value of our water resources as a full partner with domestic, industrial, and agricultural values in water quality management policies and programs.

8. Administration of water pollution control programs on State and interstate streams should continue to be the responsibility of the State agencies which therefore must be supported by adequate budgets and staffed by competent directors, engineers, scientists and related professional personnel. It is essential that the State legislatures appraise more realistically their opportunities and responsibilities in carrying out the principle herein stated and are urged to take appropriate action where necessary.

9. The administrative level of the water supply and water pollution control activities in the Public Health Service and in the States should be commensurate with the importance of this problem.

10. That State statutes and organizational structures for water pollution control should be reviewed and strengthened or revised where necessary. The following revisions were proposed in the suggested 1950 State Water Pollution Control Act as a guide for State legislation in this field.

The proposals were:

(*a*) Vest comprehensive authority in the State water pollution control agency, which would be given independent status in its organizational placement in State government;

(*b*) Insure construction of municipal treatment facilities ordered by the State agency by authorizing courts to direct all necessary steps, including bond issues, tax levies, and revenue charges if required;

(*c*) Authorize the establishment of sanitary districts to deal with local pollution control problems beyond municipal limits.

Panel III did not arrive at an agreement on these proposals.

11. The Federal Government has clear responsibilities in its working relationship with State and local governments with respect to: research, leadership in personnel training, regulatory procedures, water resources inventories and investigations, and standards of water quality.

No agreement was reached among the conferees as to extension of authority of the Federal Government in the area of water pollution control.

12. That appropriate public and private agencies mount and sustain an expanded program of public information to the end that enlightened public opinion can be brought to bear on the accomplishments, costs, needs, opportunities, and problems involved in water quality management, noting that this Conference should provide a dramatic opportunity to launch such a program.

13. There was general agreement that the public needs more information on pollution and its abatement. Government agencies and other informed individuals should make every effort to present the facts in understandable form for use by individuals, organizations, and the general media of communication. Such material should include factual information and suggested methods of attack as have been discussed by the Conference.

14. The Federal grants-in-aid program has provided a valuable stimulus to the control of stream pollution. Other methods of financing construction of sewage and waste treatment works deserve thorough study and investigation to determine the most appropriate means available or which might be made available for sound and equitable allocation of costs. Several other means of financing were suggested in one or two papers presented at the Conference. The view of the panel subcommittee was that these should be listed and appraised without any commitment on the part of the subcommittee as to which, if any, should be recommended. It did suggest that these and others unnamed should be explored at some subsequent time:

(*a*) Incentive grants from Federal and State appropriations;

(*b*) Guaranteed bonds;

(*c*) Revenue bonds;

(*d*) Marketing long-term revenue bonds under a Federal system of guarantees such as FHA-guaranteed mortgages or loans for defense production purposes;

(*e*) The creation of "Water RFC" or such Federal finance agency to discount, purchase or collateralize such bonds for loan purposes; and

(*f*) The earmarking of specific taxes, notably from Federal licensing of pleasure boats and sale of fuel to all waterborne craft, for water pollution control purposes.

15. The construction of municipal waste treatment facilities should be expanded immediately with continued increases to keep up with population growth and to abate the backlog of pollution by 1970. A similar program expansion should be applied to the wastes from industry.

16. That financial incentive should be provided to encourage industry to install needed waste treatment facilities. This may be accomplished by permitting industry, for corporate income tax purposes, to charge the cost of nonproductive waste water treatment facilities as expense.

17. Each Federal installation should be required by Congress to treat its wastes in accordance with the standards for cities and industries in the area, with 1964 set as the target date for providing minimum treatment.

18. Enlargement and extension should be made of the water quality monitoring programs now in effect, so as to reveal more adequately conditions, existing and future, in rivers and streams. We believe that the protection of the public health and the preservation of water supply sources for accepted beneficial uses require such extension and enlargement.

19. In order to facilitate assessment of the total pollution problem, it is reccommended that particular attention be given to accelerating the collection of information on industrial waste loading. The Public Health Service should coordinate collection of this information on the national level.

20. States should develop water monitoring programs for bacteriological, biological, chemical, physical and radiological quality. This work should be coordinated with the efforts of an expanded national water quality network of the Public Health Service. More data should be collected on the condition of streams both before and after water pollution abatement.

21. Provision should be made within the Public Health Service for developing the water quality criteria which are suited to application on a national basis. However, many water quality criteria are not uniformly applicable because of the effects of area usage differences, stream characteristics and other factors. State and local determinations of some criteria also will have to be made. It is recognized that periodic revision of these criteria not only will be in order, but should be sought, as new data are made available.

22. That the Public Health Service assume leadership, in collaboration with other public and private agencies, in collecting, compiling, and publishing pertinent data on the toxicity of water contaminants. This should include criteria, standards, methods of testing, and safe allowable concentrations for human consumption; also that efforts be made to stimulate toxicological and epidemiological studies to be made to determine long- and short-range effects.

23. The total national support for research in water supply and water pollution control should be increased substantially.

24. The flow of research findings on the water environment must be increased and intensified in depth as well as breadth.

25. That improved methods be developed for measuring pollution abatement progress. New engineering parameters which encompass all pollution components, as well as yardsticks for measurement of stream quality, are critically needed.

26. It should be regarded as an obligation on the part of industry to undertake basic research which will determine the biotic and other effects influencing the public welfare of the products they distribute. This should apply to detergents, insecticides, pesticides, herbicides, fertilizers, and other microchemicals and microbiologicals, and to the effects of metallic wastes such as compounds of chromium and cyanide. Where the effects of these or other health hazards or potential public nuisances are not adequately treated within industry, the Federal Government or the States must provide for and budget such research. Additional research of peculiar public responsibility includes the effect and interpretation of reducing anaerobes, nitrifying bacteria, viruses, protozoa, and other biota, and radiation hazards.

27. The flow of engineers and scientists who are competent to advance and administer the scientific, technological, and economic conservation of our water resources, including, in particular, the control of water pollution, must be increased promptly by recruitment and training of basically qualified personnel at two levels: (*a*) the professional or predoctorate level; and (*b*) the postdoctorate level.

28. The field of water supply and pollution control has become so complex that we must think more generally than in the past of a multidisciplinary approach to the solution of developing problems. This implies the introduction of representatives of many disciplines including economists and political scientists, as well as applied mathematicians and physicists to this field and the creation of requisite institutes or centers for environmental health research at which needed personnel can be brought together.

29. The capability of graduate schools or university departments of engineering and public health to produce a sufficient number of engineers and scientists who are able to deal effectively with the mounting problems of water resource control must be enlarged by support of staff, student body, and teaching and research facilities, as well as by grants-in-aid of research. Interdisciplinary research should be encouraged in particular. Because the use of personnel and the application of research lie in the public domain, the Federal Government must be expected to assume a substantial portion of the required financial burden.

30. The flow of treatment-plant operating personnel as well as engineers and scientists working in the wider field of water supply and water pollution control must be increased and their training broadened.

NOTE.—From Clean Water—"A Challenge to the Nation Highlights and Recommendations of the National Conference on Water Pollution," Public Health Service Publication No. 816.

THE 1962 BUDGET FOR WATER SUPPLY AND POLLUTION CONTROL

Mr. McCallum. The amount requested for this program for 1962 is $15,028,000, an increase over the 1961 budget of $2,885,700, of which $606,000 is for research grants and $2,279,700 for direct operations. About one-half, or $1 million, of this increase is for special work begun this year on the Great Lakes. This is an extremely important study. It will provide a blueprint for protecting the Great Lakes against increasing volumes of pollution that are inevitable with the developments this great fresh water resource and artery of commerce is bound to attract.

The remainder of the increase is for the national water quality network, research, technical services, and enforcement. The estimate for technical assistance under this item also includes administration of the $50 million construction grants program.

GRANTS FOR WASTE TREATMENT WORKS CONSTRUCTION

Mr. Chairman, a key and integral element of the water pollution control program is the grants for waste treatment works construction authorized by the Congress in 1956. The stimulatory effect of the grants is reflected in a 62-percent increase in municipal waste treatment construction.

During the 5-year period before the grants, construction averaged $222 million per year. Since the grants have been available, construction has averaged $360 million per year. This is still well below the $600 million level of annual construction necessary to provide for population growth, obsolescence of existing facilities, and elimination of the backlog of needed projects by the end of 1967. It is, however, an encouraging step toward controlling water pollution which, in the final analysis, requires the construction of abatement works.

Twenty-six hundred grant offers totaling $215 million were made as of February 15, 1961.

These grant offers have stimulated the construction of works costing $1.2 billion. The ratio of local to Federal funds remains about 5 to 1.

Recent information supplied by the States on municipal waste treatment construction points up a backlog need of $2 billion. This includes approximately 5,200 sewage treatment plants and associated interceptor and outfall sewers.

It is estimated that the $50 million requested for fiscal year 1962 will provide grants for 570 projects.

I shall be glad to answer any questions the committee may have.

Water Supply and Pollution Control

GRANTS TO STATES AND INTERSTATE AGENCIES

Mr. Fogarty. The largest increase, $2,885,700 is for water supply and pollution control. The first activity is grants to State and interstate agencies where you are asking for $3 million. This is just what you had in 1961, isn't it?

Mr. McCallum. Yes, that is the statutory ceiling.

Mr. Fogarty. I notice that every interstate agency is getting an increase except New England. What have you got against New England? You are reducing its grants.

Mr. McCallum. That is based on the formula in the act that applies to States. To the interstate agencies these funds are apportioned on the same basis as they are to the participating States. I note that there is some difference in the States, too, following the 1960 census.

That would be the only reason that I know of.

Mr. Fogarty. We in New England have had a problem in trying to get an interstate compact. Would that have anything to do with this apportionment?

Mr. McCallum. No, this apportionment is made on the basis of the apportionments of the States that make up the compact.

Mr. Fogarty. Do you know about this problem? One or two States have not signified their intention of approving this interstate compact.

Mr. McCallum. In general, yes. That is one of our responsibilities under the act, to encourage compacts, and we have been working——

Mr. Fogarty. I believe Rhode Island, Massachusetts, and New Hampshire have agreed, but Maine and Vermont have not?

Mr. McCallum. I believe that is correct. We could get that information, sir.

Mr. Fogarty. Why don't they want to join?

Mr. McCallum. I don't know.

Mr. Fogarty. Can we go along without them?

Mr. McCallum. I think the philosophy is that such a compact, to be effective, should have the participation of States with a common interest. I happen to be a commissioner on the Tennessee compact, which is really not effective as yet, and some of the States haven't ratified that as yet either. But we are hopeful that within the next couple of years or so that will be in operation. The reports I have heard from a member of the New England Commission on our Water Pollution Advisory Board—Mr. Wise of Connecticut—at a recent meeting seemed to be optimistic that this will go through.

Mr. Fogarty. He thinks it will. There isn't anything you can do to help it through?

Mr. McCallum. Well, we are helping any way we can working with the Justice Department and the Budget Bureau.

RESEARCH GRANTS

Mr. Fogarty. You have an increase of $606,000 for research grants. Tell us in general the type of research, who is doing it, what results you have, and why you need this increase.

Mr. McCallum. The types of projects that we are now getting are on a somewhat broader base, something we have been trying to encourage in the departments of universities other than just the schools of engineering, which were formerly the main source of such grants. For example, the chemistry departments and the physics departments, and the biology departments.

I believe there are 43 schools participating this year, and we expect to have 150 continuing grants from fiscal years 1961 to 1962, and this increase would support an additional 58 new ones for 1962.

RESULTS

Mr. FOGARTY. What results have you been able to get?

Mr. McCALLUM. One recent result is from the Massachusetts Institute of Technology on the effects, the adverse effects, of toxic materials in sewage on sewage treatment, which is a biological process, and the concentrations that will result in lowered efficiency, which, of course, means that the plant will do a less effective job in preventing water pollution.

Another study going on at Washington State University has to do with the persistence and the effect on aquatic life of insecticides and some of the new agricultural poisons in natural waters, and the extent to which they have hydrolized or iodized and become less dangerous.

Another study going on which has made preliminary reports is on return irrigation water. Some kinds of pollution of a new dimension in water pollution that we haven't had to worry about as much in the past have appeared. These are materials which are returned to our water courses with water that has been used for irrigation, particularly when they are in combination with some of the new chemicals that are used for weed control and pest control.

This work can very well be done at such universities, because they have the scientists and the community of knowledge to attack these difficult pollution problems.

Another piece of research that is of interest is—it is one on the effects of certain types of fungus that are formed. The project is at Washington State University at Pullman. Certain types of fungus that are formed from certain pollutants, and their secondary effect on aquatic life, which, in turn, reduces the stream's natural purification processes.

DIRECT OPERATIONS

Mr. FOGARTY. The major part of your increase, $2,279,700, is for your direct operation. What are some of the major problems there?

GREAT LAKES AND ILLINOIS WATERWAYS

Mr. McCALLUM. Half of that increase goes for work on the Great Lakes and the Illinois Waterways. That is being done under a section of the act that requires the Surgeon General, in cooperation with the States and municipalities and industry, to develop comprehensive programs for the prevention and control of pollution.

Our priority—ultimately we intend to cover all the basins in the country—our priority is based on where the information is needed in connection with the responsibility of other Federal agencies. In this case, it is the Justice Department and the Supreme Court.

The project was started last year under an appropriation of $500,000 from the Congress, and the initial stages of it are limited to the south end of Lake Michigan and the Illinois Waterway, 325 miles from Lake Michigan to the Mississippi River. We have collected and are collecting factual data from the four States involved, from the cities and from the industries, and are supplementing that with actual observations in the field where necessary to fill in the gaps.

And I might say that the crux of this particular pollution problem, which is a very large one that is duplicated in a good many other parts of the country, is that Chicago, the Nation's second largest city, is located right on the divide between two watersheds, the shallow water of Lake Michigan on the one side, and the very small headwaters of tributaries of the Mississippi on the other. This was a problem even before the turn of the century, and it was recognized at that time, when Chicago had one of the highest typhoid rates in the world.

And about 1900 they dug a ship and sanitary canal to reverse the flow of the Chicago River from Lake Michigan to what we know as the Illinois Waterway to take water from the lake to carry away the wastes from the Chicago metropolitan area.

Litigation was begun almost immediately by the State of Missouri, contending that wastes from Chicago would endanger the water supply of St. Louis. In addition litigation by lake States was instituted to limit the diversion of lake water. The Supreme Court now has before it the question of whether diversion can be reduced below the now authorized 1,500 cubic feet per second.

So that in our plans we are having to look at this outlet of Lake Michigan into the Illinois Waterway to get the answers to the questions that the Justice Department is now in need of.

After we get the factual data, the second phase of the project will begin with sampling on the Illinois Waterway. We have established 63 sampling stations between Lake Michigan and the Mississippi River. And we are working with the Corps of Engineers on plans for development of floating sampling stations and current measuring stations in Lake Michigan.

We don't know, for example, the lake currents as we do know the currents in a moving stream. There is some indication that there is a sort of counterclockwise, large whirlpool in the middle of Lake Michigan, perhaps toward the southern end, that is displaced very slowly, that wastes entering that area might persist there for very long periods of time.

In addition to the Illinois Waterway, part of the second stage of the program will be observations in about, we think, 8,600 square miles of the southern portion of Lake Michigan, to determine what the currents are and what happens to the wastes that are now getting in there, and what the effect would be, to predict what the effect would be from additional waste loadings, and come up with a plan or recommendation as to what additional waste loadings or additional waste treatment may mean in the south end of the lake.

PROBLEMS OF WASTE IN THE DELAWARE RIVER BASIN

Mr. Fogarty. The Secretary of Health of Pennsylvania has written me a letter. They are very much concerned because they have a very serious problem in the Trenton-Philadelphia-Wilmington area to handle the waste loads. Do you know of their problem?

I will put the letter in the record.

(The letter referred to follows:)

March 11, 1961.

Dear Mr. Fogarty: The comprehensive study of the Delaware River Basin headed by the Corps of Engineers, and the interest in establishing a compact, clearly indicates the need to find solutions for the water resources problems of the Delaware River Basin.

The water pollution studies, which were a part of the comprehensive corps study, need to be further supplemented so that we may find even better means to abate pollution in the tidal estuary portion of the basin. There is a question as to the ability of the estuary in the Trenton-Philadelphia-Wilmington areas to handle additional waste loads without creating serious problems.

It is my understanding that the Public Health Service is willing to undertake further studies in cooperation with State and interstate agencies as authorized by section 2 of the Federal Water Pollution Control Act. The Pennsylvania Sanitary Water Board strongly supports such an endeavor.

It is our understanding that there is no provision for this in the Federal budget request for the fiscal year 1962. We recommend that appropriate funds for this important project be made available to the Public Health Service for the fiscal year 1962.

Very truly yours,

C. L. Wilbar, Jr., M.D.,
Secretary of Health.

Mr. McCallum. The Delaware River is one of the 26 basins we plan to study.

STATE CONTRIBUTIONS FOR RIVER BASIN STUDIES

Mr. Fogarty. What is your policy regarding contributions from the States that stand to benefit from these studies?

Mr. McCallum. Well, in the studies we have participated in so far, the States have helped. They have consistently helped since we began in the Arkansas–Red River project, and it would have cost us considerably more if we had had to do it all ourselves. And the way our act is written, it makes clear that these comprehensive programs are to be developed in cooperation with the States and interstate agencies and municipalities and industries.

I might add that the Surgeon General in January, I believe it was, appointed a committee of 13 representatives of States, industries, and municipalities and the Chicago Sanitary District to work with the Public Health Service on the Great Lakes-Illinois Waterway study. We had a meeting in which Dr. Anderson and I were present in Chicago on March 10 with this committee, the first meeting. And one of the purposes of the meeting was to elicit the support and assistance of these other groups in the basin. We feel that is very important, because when the technical work is done and the final plan is finished they are the people who will have to put it into effect and see that it works.

Mr. Fogarty. You do not have a formula of any kind where the States contribute so much?

Mr. McCallum. On this sort of study? No.

Mr. Fogarty. Suppose you had a six-State area and only one State was going to contribute, would you still feel obligated to that particular area with the limited funds that you have?

ARKANSAS-RED RIVER PROJECT

Mr. McCallum. One of the criteria that we use, in addition to that of serving other Federal agencies, is the attitude on support of the people in the area. For example, on the Arkansas-Red River project, we have had very substantial support from everyone—the chambers of commerce, the industrial organizations, the farm organizations, municipalities, and States.

Mr. Fogarty. And the Speaker of the House of Representatives?

Mr. McCallum. I understand he is interested in it.

And that is one of the criteria that we will continue to pay attention to, particularly for this reason: that they are the ones who are going to have to implement any plan that is devised.

And, if they are that much interested, I feel confident that we will have good support and help.

Mr. FOGARTY. There was a great deal of interest down there, I know.

What is the status of that project?

Mr. MCCALLUM. It is coming along very well.

Mr. FOGARTY. When do you expect to finish it?

Mr. MCCALLUM. We will be finished—we expect to have all of our recommendations made as of January 1, 1963, and we have made a good many already, so that the corrective measures would not have to wait until we are entirely finished.

Mr. FOGARTY. Do you have sufficient funds in this budget to complete this project in fiscal year 1962?

Mr. MCCALLUM. Yes, sir. As a matter of fact, we asked for less than we did last year, and it is coming along very well.

ENFORCEMENT ACTIVITIES

Mr. FOGARTY. You are requesting $1,647,000 for enforcement activities. That is a slight increase. What is this needed for?

Mr. MCCALLUM. In the enforcement activities the increases are, first, for the Colorado River project, which was instituted last year at the request of the seven States in the basin. We are doing that as an enforcement action, although in many respects it is comparable to one of the comprehensive programs.

As we are progressing we are collecting data in such a way that we can use it for law enforcement. There will be conferences held at interstate junctures where there is pollution indicated affecting the health and welfare of the people in a State other than where it originates.

That project is well started. We have about 25 or 30 sampling stations from Wyoming to the Mexican border where we are collecting bottom sediments for certain chemical and biological tests, including that for radioactive matter; and we have several additional stations for water samples in the upper tributaries, a good start on factual data from the States, and next year with the increase, we hope, in addition to these activities, to give attention to return irrigation flows and also some calculation on what return irrigation flows resulting from proposed Federal projects in the upper basin may mean.

Another portion of the increase is for Federal installations. We budget that under enforcement. A year ago in May the President asked the Secretary of Health, Education, and Welfare to take the lead in gaining information on the pollution situation from Federal installations. There are some 13,000 Government-owned installations and about 38,000 leased installations where the Government does have responsibilities. There has not been, heretofore, information on what the facilities were, what the extent of the problem was, or what should be done about it. That is what we are doing this year. Next year we hope to get into some of the corrective measures where the Congress proposes that Federal installations be included in the report on conferences and enforcement hearings under the Water Pollution Control Act. They are not covered in the present act.

The other part of the increase for law enforcement is for what we call the general program, and that is to follow through on the cases where we have had conferences, and corrective measures are supposed to go forward, such as St. Joseph, Mo., which is holding a bond election April 11. We hope this will succeed because that is the only case that has been turned over to the Justice Department.

I would like to say that our philosophy of enforcement is to try to obtain corrective action to control pollution in any way we can without using the enforcement procedure, or correcting it in the early stages of the enforcement procedure without going to court, if possible.

Another part of the work which we are doing in enforcement on the general program is to obtain information on some 2,000 interstate water areas to see what the situation is as of any particular time, and the progress that the States and the localities or industries may be making on handling it.

The Surgeon General does have responsibility under the act to call a conference on his own volition. And these dockets, as we call them, constitute our surveillance on the situation before we are called in to determine on a going, continuing basis whether or not there is an indication of a need for the Federal Government to do more.

We have now, I believe, dockets on about 50 of these 2,000 interstate water areas and next year we expect to get that up to 150.

This does not in general involve fieldwork, but holding a conference with the State or interstate agency—that is not an enforcement conference but an understanding, rather, that we are agreed on the facts and on what has been done about the situation, or whether or not anything further needs to be done.

RESEARCH CONTRACTS

Mr. Fogarty. The summary table which takes in all environmental health activities indicates that you have about $3 million budgeted for research contracts. What type of research is this, and why couldn't it be handled through the regular grant process?

Mr. Ackerman. Many of these contracts are in the air pollution program, although all of our programs in environmental health use the research contract to obtain a particular competency or skill available at certain research institutions. I have a list of contracts by the various programs which can be filed which are listings of the types of contracts that we are working now, and some general fields in which we plan to contract in 1962.

Mr. Fogarty. Why couldn't this all be handled under the regular grant process?

Dr. Anderson. Some of them, Mr. Fogarty, are for such things as the development of instruments that might be used for measuring, say, air pollution, or radiation, or in some other medium—water, for example. For these, we have specifically in mind what it is that we want. So, then, with this in mind we go out and seek a specific competency from a private institution or another governmental agency or university, to enlist their talents to produce what it is that we need to conduct our direct operations.

Mr. Fogarty. What does the overhead allowance average of these contracts?

Mr. ACKERMAN. With regard to the overhead allowance, the general policy, I believe, is to follow the armed services procurement general practice. The Budget Bureau a year or so ago set up a general policy that at those universities that were doing a substantial amount of governmental research work, and where the larger part of it is with the Department of Defense, they worked out a standard policy guide for the determination of overhead allowance which relates it, I think, essentially to the actual cost.

Perhaps Mr. Kelly can add something to that.

Mr. KELLY. In connection with all of our research contracts on universities, the departments' procurement manual calls for the utilization of the Budget Bureau Circular A–21, which is the one that you are familiar with, and which gives the method of measuring indirect cost associated with direct cost. And as Mr. Ackerman has said, for most of these cases the military give us their determination in connection with their contracts, and we review and apply it.

My guess would be that the average indirect cost would be somewhere between 25 and 30 percent, but I don't have it precisely. The range would be much greater. The average, I think, would fall between 25 and 30 percent.

GRANTS FOR WASTE TREATMENT WORKS CONSTRUCTION

Mr. FOGARTY. Now, for grants for waste treatment works construction, the request is for the full amount authorized this year, $50 million.

Mr. McCALLUM. That is correct, sir.

STATES NOT USING ALL FUNDS IN PAST

Mr. FOGARTY. I notice you don't expect to use the full authorization in 1961. What States aren't using their full allotment?

Will you supply that for the record?

(The information requested follows:)

State and territories using less than their full allotments: Since the 1961 appropriation will be available through 1962, it is not known which States will not use these 1961 funds. The appropriation for 1959 is the latest one that has been closed, because each year's appropriation remains available for 2 years. In 1959, the total grant obligation was $46,815,573, from new obligational authority of $46,816,000. Of this amount, $45 million was provided in the basic appropriation and $1,816,000 was provided by a supplemental appropriation. The regular appropriation act provided that allotments to States be made on the basis of $50 million. Nine States and territories whose allotments totaled $6,575,925 did not use their full allotments; they were: Alaska, Puerto Rico, the Virgin Islands, Mississippi, Nevada, Rhode Island, South Carolina, South Dakota, and Wyoming. The total amount of the authorized $50 million that these States did not use was $3,184,427.

APPLICATIONS ON HAND DECEMBER 31, 1960

Mr. FOGARTY. Why is it that some States had on hand last December 31 more applications than they would be able to finance by the end of 1962, whereas other States had none on hand?

Mr. McCALLUM. Well, some States have a very substantial backlog.

(The table being referred to follows:)

Analyses of Federal funds available for waste treatment works construction in fiscal year 1962

	Federal share of approved applications in State offices forwarded to DHEW regional offices as of Dec. 31, 1960 (1)	Federal share of all applications on hand in State offices, approved or not as of Dec. 31, 1960 (includes amount shown in col. 1) (2)	Unobligated Federal funds available to State for additional applications through fiscal year 1961 as of Dec. 31, 1960 [1] (3)	1962 State allocations (4)	Total, cols. 3 and 4 (5)
Total	$21,917,116	$53,499,554	$33,699,774	$50,000,000	$83,699,774
Alabama	87,690	727,950	698,524	1,081,325	1,779,849
Alaska	147,737	507,737	824,300	376,725	1,201,025
Arizona	----------	----------	315,649	627,600	943,249
Arkansas	511,204	511,204	973,516	949,775	1,923,291
California	----------	5,159,910	1,021,597	2,499,925	3,521,522
Colorado	367,312	373,462	24,660	662,275	686,935
Connecticut	----------	137,160	475,563	657,000	1,132,563
Delaware	195,000	195,000	396,038	359,125	755,163
District of Columbia	----------	97,692	690,605	405,650	1,096,255
Florida	656,063	3,071,822	976,640	1,129,950	2,106,590
Georgia	250,000	250,000	502,424	1,121,500	1,623,924
Hawaii	----------	----------	827,582	510,700	1,338,282
Idaho	188,876	188,876	680,550	590,025	1,270,575
Illinois	263,177	1,940,746	333,666	1,723,300	2,056,966
Indiana	3,928,991	4,072,391	25,249	1,059,125	1,084.374
Iowa	2,221,852	2,221,852	914.040	828,325	1,742,365
Kansas	----------	----------	64,036	743,575	807,611
Kentucky	118,975	1,187,377	776,942	1,003,275	1,780,217
Louisiana	1,949,860	3,220,430	322.365	1,000,225	1,322,590
Maine	----------	----------	1,254,426	633,900	1,888,326
Maryland	----------	607,431	439,043	805,175	1,244,218
Massachusetts	936,525	936,525	978,014	1,071,400	2,049,414
Michigan	108,000	5,218,483	1,103,802	1,462,575	2,566,377
Minnesota	257,762	257,762	1,076,888	915,800	1,992,688
Mississippi	----------	----------	1,357,842	1,100,250	2,458.092
Missouri	72,600	110,196	125,635	1,015,900	1,141,535
Montana	250,000	479,314	162,983	527,675	690,658
Nebraska	71,295	142,540	157,361	634,550	791,911
Nevada	----------	----------	584,197	367,650	951,847
New Hampshire	236,676	236,676	975,772	530,800	1,506,572
New Jersey	1,089,570	1,339,570	2,157	1,171,500	1,173,657
New Mexico	377,933	377,933	183,630	621,375	805,005
New York	1,060,609	1,492,109	1,771,203	2,635,650	4,406,853
North Carolina	----------	7,193,760	2,471	1,236.250	1,238,721
North Dakota	187,000	187,000	940,494	638,050	1,578,544
Ohio	----------	1,355,935	66,004	1,710,700	1,776,704
Oklahoma	1,043,318	1,043,318	402,485	820,325	1,222,810
Oregon	----------	811,140	63,984	662,625	726,609
Pennsylvania	488,000	488,000	329,939	1,951,250	2,281,189
Rhode Island	250,000	250,000	1,036,904	531,875	1,568,779
South Carolina	23,422	23,422	1,950,839	1,006,675	2,957,514
South Dakota	----------	----------	1,152,332	641,875	1,794,207
Tennessee	----------	----------	132,606	1,079,700	1,212,306
Texas	2,472,023	3,060,146	298,412	1,780,000	2,078,412
Utah	----------	436,583	333,602	602,900	936,502
Vermont	----------	----------	540,395	557,725	1,098,120
Virginia	261,395	574,329	589,621	1,034,075	1,623,696
Washington	----------	311,500	268,163	782,500	1,050,663
West Virginia	51,030	909,052	109,459	786,875	896,334
Wisconsin	1,793,221	1,793,221	1,228	966,075	967,303
Wyoming	----------	----------	529,910	458,075	987,985
Puerto Rico	----------	----------	2,294,527	1,123,850	3,418,377
Virgin Islands	----------	----------	1,639,500	805,000	2,444,500

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[1] Based on allotment total of $50,000,000.

NOTE.—Agencies report additional applications in preparation by communities which will require $90,279,733 of Federal funds.

Mr. **Fogarty.** Some of them didn't have any on hand.

Mr. **McCallum.** My home State of Michigan always has 75 to 100.

Mr. **Fogarty.** They have always been a little bit ahead of most of the others on this problem, haven't they? How about California?

Mr. **McCallum.** It is another State which has had a very large number of——

Mr. **Fogarty.** What about Kansas? They didn't have any on hand.

Mr. **McCallum.** I am not acquainted with the situation in Kansas.

Mr. **Fogarty.** What about South Dakota, Tennessee and Mississippi; this table shows none for them.

Mr. **McCallum.** Mississippi has under the formula a fairly large apportionment or allotment for the size of the State. For example, Mississippi doesn't get anything like the money that the State of Michigan does under the formula, but there are no provisions in the present act to reallocate these funds, although such amendments——

Mr. **Fogarty.** And you are talking about Mississippi now?

Mr. **McCallum.** Mississippi?

Mr. **Fogarty.** Yes; they don't have any applications on hand, according to this table.

Mr. **McCallum.** They have been using their money up until this year, if they are not using it this year, this is the first year.

Mr. **Fogarty.** Do you have the same table I have?

Mr. **Ackerman.** Mr. Moyer just supplied us with a copy, but I don't think that we have had a chance to analyze it.

Mr. **Fogarty.** That seems strange. Where did we get this table?

Mr. **Kelly.** We supplied it to you, sir, we obtained it from the Public Health Service.

Mr. **McCallum.** Some of the States—now I believe certain States in New England don't make their final determination on funds during the fiscal year until about this time when they have their town meetings. That doesn't mean that they won't use the funds, but they have not made——

Mr. **Fogarty.** That may go as far as Vermont and Maine are concerned, because they are the only States in New England which show no applications on hand December 31.

Mr. **McCallum.** This list is as of December 31, and I know that some of the States do not have their hearings and their priority determinations completed at that time.

Mr. **Ackerman.** Mr. Chairman, Mr. Dunning informs me that these dotted lines do not necessarily mean that they do not have any applications, but rather they have not reported as of December 31.

LAG IN GETTING INFORMATION FROM STATES

Mr. **Fogarty.** It seems to me there should have been some indication on the table to tell us that. Why is it that all these other States have reported, and these 10 or a dozen States haven't? Mr. Dunning, go ahead if you have the answer.

Mr. **Dunning.** Within this grant proceeding the States determine the priority of certification among numbers of applicants. Quite a few of them accumulate a number of applications or tentative applications, and then make their priority determinations on one or two occasions in a year. If they take off a tabulation as of a given date, you never have a complete picture for the whole country, because some of the applications are being held in States pending a priority determination.

Mr. Fogarty. What do you mean by "Federal share of all applications on hand in State offices"? That is in the second column.

Mr. Dunning. That would be the grant money for all—it is different from the first column, which is for applications that States have approved and forwarded, and this second column is applications that States have reviewed but not approved as yet. And some of them had not reported on December 31.

Mr. Fogarty. That means you are halfway through the fiscal year, and you don't know what they are going to ask for or even know the amount of applications they have received. Do you mean they could go up until May of this fiscal year before they give you an estimate of what they are going to use?

Mr. Dunning. That is right. Of course, as a general rule, they don't, because we arrange with them to cover these.

Mr. Fogarty. I see.

Mr. Kelly. Mr. Chairman, there is a note on the bottom of that table which might be of interest to you which states that all these States have not received formal applications, and yet they were able to report that they had knowledge of communities that were in the process of preparing applications that total $90 million.

PROPOSED LEGISLATION

Mr. Fogarty. The new legislation being proposed calls for an appropriation of $100 million, is that right?

Mr. McCallum. One bill on which hearings were held last week proposes $125 million.

Mr. Fogarty. $125 million. That must be the Blatnik bill.

Mr. McCallum. Yes, hearings were concluded last Thursday.

Mr. Fogarty. The $100 million bill was the one we passed last year.

Mr. McCallum. Yes. The construction and——

Mr. Kelly. Kennedy's message recommended the doubling.

Mr. Fogarty. And the Blatnik bill is $125 million?

Mr. Kelly. Yes.

Mr. Fogarty. $25 million more than the President asked for?

Mr. Kelly. Yes.

Mr. Fogarty. Did you have something to say, Dr. Anderson?

Dr. Anderson. Yes. With regard to the allocations to the States and their obligations of these funds, it is a rare State that doesn't obligate its funds, and for those that don't completely obligate them, their unobligated balances are distributed to other States for their projects——

Mr. McCallum. That would be allowed in the Blatnik bill.

Dr. Anderson. But this is why the obligational authority now is at the rate of $50 million a year.

Mr. Kelly. We average about $47½ million in obligations, under the $50 million authorization.

Mr. McCallum. We estimate that we will be about a million dollars short on the appropriation that will expire June 30 of this year.

AIR POLLUTION—ARTICLE FROM HOUSE BEAUTIFUL

Mr. **Fogarty**. I have an article on air pollution problems that appeared in House Beautiful magazine in January of this year.

The man we had enforcing air pollution regulations and dealing with these problems in Rhode Island thought it was a good article. He did a real good job in Providence.

I am going to ask that this article be included in the record at this point.

(The article referred to follows:)

How To Protect Yourself From Air Pollution

(By Eugene A. Sloane, editor, Air Engineering)

FOUR WAYS TO SAFEGUARD YOURSELF—AND YOUR COMMUNITY

1. *Cut down the pollutants you yourself add to the air.*—Stop smoking. Don't burn leaves. Use only the most efficient home incinerators. Keep your car's engine in top shape to cut down exhaust fumes. Shut off the engine when stuck in traffic. Add exhaust-control devices as they are perfected. Add lint traps to automatic laundry dryers, grease traps to exhaust fans.
2. *Clean the air inside your own house.*—Add charcoal filters, electrostatic filters, central or room-size air-cleaning devices. Change your furnace filter regularly. Use negative-ion generators to relieve "stuffy" air. Use respirator masks if you're doing dust-producing work (power sanding, spray painting).
3. *Take special precautions if you live or drive in a real smog belt.*—Make year-round air conditioning, with air cleaned by electrostatic precipitation, your No. 1 requirement. If you have to drive constantly on smoggy highways loaded with auto fumes, wear a respirator in the car.
4. *Join with others in community organizations to fight air pollution.*—Start a citizens' committee, if none is in your town. Affiliate with national organizations. Push hard for smoke-control ordnances. Report violations to proper authorities. Become a community nuisance—it's the only way.

The subject of air pollution is not new in the world. But what is new is that a chemical linkage has been discovered between the pollutants in the air and pollutants in other phases of our lives. The chemicals present in industrial polluted air are the same or closely related hydrocarbons that are present in tobacco smoke, smoked meats and fish, burned fats, and automobile exhausts. The cumulative effects of all these sources add up to a condition that must be faced, or we will poison our most necessary physical act—breathing.

Even if you live in the remote vastness of Alaska, or on the sunny shores of Waikiki, you can't escape breathing polluted air. Sulfur dioxide air pollution, for example, has reached worldwide proportions, according to studies made during the last International Geophysical Year.

Some of the air pollution facts are well known: that nylon stockings disintegrate, that white house paint can turn black overnight, that pollution can decay marble in New York, peel chrome off car bumpers in Chicago, poison plants in Florida, kill cattle in Oregon. Air pollution has been blamed for the deaths of 4,000 people during the 1952 London smog episode. Deaths of 20 people and the illness of 5,910 people (42 percent of the city's population) in the Donora, Pa., incident in 1948 were blamed on air pollutants from factory smokestacks.

The thousands of tons of dust that daily fall out of the skies over our big cities contribute heavily to the soiling of draperies, dust collection on furniture, soot on paint finishes and on your automobile.

The smog of southern California makes the eyes water, causes stomach upsets, worsens chronic respiratory ills. During autumn smog periods, teachers complain that school children are less alert, get lower grades.

Air pollution hurts most those least able to resist its inroads * * * the new born, the ill. the aged. According to Dr. Peter V. Hamill, Chief of the U.S. Public Health Service's investigation into the relationship between cancer and air pollution, aerial garbage contributes to chronic bronchitis, cardiovascular (heart) disease, asthma, and cancer of the lung and stomach.

In New York City, visibility has been so reduced by filth-laden air that airplane flights have been canceled, ferry boats have collided, schools and industrial plants have had to be closed, and cars have collided by the score. During these episodes, New York's hospitals are jammed by patients with respiratory ailments.

Even Washington, D.C., the country's least industrialized city, has its air-pollution troubles. Citizens on their way to work last summer began to weep in unison when a combination of still air and a layer of warm air above caused a California-type inversion that "locked in" exhaust fumes from 200,000 commuters' cars.

Medical and public health investigators, including Dr. Leroy Burney, Surgeon General of the United States, say that cities with the heaviest air-pollution loads tend to rank high in death rates. Dr. Burney says: "We know that lung cancer death rates in the largest cities are twice as high as those in nonurban areas."

In a vast 10-year study of lung cancer among British emigrants to New Zealand, the death rate from lung cancer was 30 percent higher among the British born than among native New Zealanders, despite the fact that the New Zealanders smoke even more than the native Britons.

Britishers who emigrated to New Zealand after the age of 30 had a lung cancer death rate 75 percent higher than that found in native New Zealanders. Their years of exposure to the smoggy, dirt-laden air of England was blamed for predisposing the British emigrants to lung cancer, long after they had left their native soil.

What's in the air that can harm you? One of the most common pollutants, and one which has been proved to cause cancer in laboratory animals, is a byproduct of incomplete combustion.

Incomplete combustion produces unburned hydrocarbons that contain an ingredient called 3,4-benzpyrene. According to Dr. Wilhelm C. Hueper, Chief of the Environmental Cancer Section of the National Cancer Institute, minute amounts of 3,4-benzpyrene have caused cancer in laboratory animals.

What are some of the sources of incomplete combustion containing the cancer-causing agent, 3,4-benzpyrene? It is found in the fragrant smoke of burning leaves, in the lethal fumes of auto exhausts, in the black plume of smoke from home or factory chimneys, in cigarette smoke.

If you live in a big city and are not a smoker, you still inhale about 16 times as much 3,4-benzpyrene as the country dweller who smokes a pack of cigarettes daily, says Dr. Eugene Sawicki, of the Robert A. Taft Sanitary Engineering Laboratory.

We inhale, if we live in a big city, about 40,000 times the amount of 3,4-benzpyrene capable of producing cancer in mice, according to Dr. Hueper.

About 500 new chemical compounds are introduced into our environment each year, and many of them find their way as complex combinations into the food we eat and the air we breathe. Waste products, dusts, fumes, mists, acids are dumped wholesale into the air of our industrial cities.

Metallic fumes and dusts from lead, vanadium, arsenic, beryllium, and fluorine are just a few of the compounds in the air you may be breathing at this moment.

If you're healthy, says Dr. Hamill, you can easily tolerate the modest amount of contaminants you breathe on the job every 8 hours. Or you can stand the daily whiffs of car exhaust, the little bit of amino triazole in a spoonful of cranberry sauce, any of 18 lipstick coal tar dyes, and the pesticides that contaminate the food you eat.

But add all these poisons up, says Dr. Hamill, and you have an aggregate of environmental insults that can harm the healthiest of us, sooner or later.

Will the air we breathe get even dirtier than it is today? The evidence points to a positive "yes" unless we do something about it now. Already there is a vast metropolitan complex, almost one huge city, all the way from Boston to Washington, D.C. Cities are growing bigger, and industry is adding hundreds of new chemicals and new manufacturing processes every year.

By 1970 there will be over 90 million cars on the road as against 68 million now. About 3.5 tons of pollutants are produced daily for each 1,000 cars.

Air pollution, according to a recent report, costs every person in the United States $65 per year, a total of $7½ billion. According to Carl A. Lindstrom, of the U.S. Public Health Service, air pollution caused over $200 million dollars damage to real estate in 1959.

Air pollution knocked out a huge powerplant in North Carolina recently, plunging thousands into darkness. Airborne acids ate away powerline insulation, shorting out main cables.

The telephone company has to protect its platinum-coated relay points in central station buildings from airborne corrosives, by special filters. This costs them a great deal of money which eventually is added to your monthly bill.

WHAT YOU CAN DO ABOUT IT

The air pollution problem isn't entirely hopeless, however. Our children need not grow up in an atmosphere (literally) poisoned by subtle, invisible, health-stealing gases, dusts, mists, and fumes.

There's a lot you can do about air pollution—by reducing your own contribution to it, by protecting yourself from other's pollutants, and by participating in your city's air-pollution control efforts.

What do you do that pollutes the air? Plenty, says Detroit's air-pollution control chief, Morton Sterling. About 40 percent of all air pollution in Detroit, he states, comes from nonindustrial sources.

Did you burn your leaves last fall? If so, you and thousands of your neighbors added literally tons of unburned hydrocarbons to the air in your immediate neighborhood.

Do you have a gas- or oil-fired incinerator? If so, be sure you know how to operate it so it burns free of smoke and odors. Don't send a young child out to stuff it with wet garbage. The best designed incinerator is no better than its operator.

If you're stuck in traffic, shut off your idling motor after 3 minutes. An idling motor spews far more unburned hydrocarbons into the air than a motor running at full throttle.

Keep your motor well tuned, spark plugs and points clean and properly adjusted. A top-performing motor emits up to 12 percent less hydrocarbons than the same motor with fouled plugs and burned points. If your car leaves a smoke screen behind it, have the motor overhauled.

A new gadget that is claimed to reduce harmful auto exhaust hydrocarbons by about 40 percent will be on many of the new cars shipped to California this year. You can have one installed on your car for from $8 to $15 at your garage or service station. It's called a crankcase blow-by unit and it pipes fumes from your crankcase vent pipe back into your motor, via the carburetor. The unit is also said to save gas by returning burnable hydrocarbons to the engine.

If your clothes drier is the type with an outside vent, you spread lint all over the landscape every time you dry a batch of laundry.

You may think your contribution is small. Try going outside and watching how much lint you discharge, and how far the wind takes it. Add to your dryer those of the thousands around you and you have a nuisance source. An auxiliary lint trap on your dryer can help the problem. Ask your plumber or dryer serviceman.

You can also keep from poisoning yourself, as well as your neighbors, from another source of cancer-causing fumes. A survey recently made by the California State Health Department showed that the occupation with the highest incidence of lung cancer was that of professional cooks and chefs. The suspected cause: fumes and smoke from frying and charring grease-laden foods, which create polycyclic hydrocarbons heavy with 3, 4-benzpyrene. (See "The Last Word on Meat Cooking," House Beautiful, August 1958.)

A range hood over your kitchen stove, with an exhaust fan of at least 600 cubic feet per minute capacity, will pull harmful cooking fumes and odors away from your breathing zone. But you should add a grease filter to your range hood, to keep cooking odors and fumes from outside.

If you burn coal for home heating, be sure to use a low-sulfur-content variety. The air over Pittsburgh was dramatically cleaned up when citizens changed from sulfur-laden soft coal to a clean-burning low sulfur coal, according to Emerson Venable, a Pittsburgh consulting engineer, who helped research his city's problem.

If you own a vacant lot, cut down your weeds during hay fever season. If your land is bare, sow it with low-cost rye seed to keep exposed topsoil from blowing.

If you've ever been to Madison Square Garden or to a football game on a fall day when the air was still, you've seen the choking cloud created by 100,000 burning cigarettes. Smoking, says Dr. Hamill, is a "highly personalized form of self-fumigation." Put more bluntly, it is a severe form of personalized air pollution. San Francisco smokers are said to put 300 tons of irritants per day into the air by smoking alone.

HOW TO PROTECT YOURSELF

What can you do to protect yourself from the polluted air you live in? Most obvious, of course, is to seal off your house, leave storm windows on all year, and install air conditioning. Since air pollution is worse during spring, winter and fall, sealing off the house isn't necessary, though air conditioning can be a boon.

To your air-conditioning system or to your forced-warm-air heating system, you can add activated charcoal filters to trap organic fumes such as unburned hydrocarbons. To the same systems you can also add electrostatic filters, which will keep the house clear of cigarette smoke—even during a club meeting.

A new air-cleaning unit recently available, which can be added to your warm-air furnace, is a real smog killer. It washes the air, humidifies it during winter, traps dirt and odors. It's costly, though, and may set you back nearly as much as the furnace itself.

A low-cost electrostatic filter introduced requires no alterations to the furnace and can be installed in the space occupied by your old mechanical filter.

Don't try to vacuum-clean your dirty mechanical furnace filters. You won't get all the dirt out, and filter efficiency will be greatly reduced when you put them back. Replace them with new filters.

Activated charcoal filters can be a real blessing, especially if you live near a source of odors, or in a city whose main industry is chemical processing or petroleum refining. In Los Angeles, downtown buildings equipped with activated charcoal filters advertise smog-free offices to prospective tenants and employees alike.

Before adding activated charcoal filters to your present forced-warm air furnace, better check with your furnace man. You may need a larger blower motor because the charcoal filters impose more resistance to airflow through the furnace.

If you have a wet heat system (steam or hot water), you can install a room-size filter unit between normal room stud spacing to filter dust and remove odors. One such unit has a bed of activated charcoal and a mechanical filter, through which a blower continually forces room air.

An electrostatic furnace filter may be a good idea if you live near a hospital. Hospitals are being eyed by medical people as sources of "clouds" of staphylococcus aureus, the dread, drug-resistant bacteria that is a product of this age of antibiotics. Students at an eastern university, who live near a hospital, recently came down with an epidemic of staph aureus infection.

So-called air purifiers (small, box-like affairs), with imposing names, as presently designed, are of little or no use in dispelling odors or for killing germs for that matter. They have a tiny fan that moves barely more air than you could with a small hand fan. And if they generate ozone, you may be in for trouble. Ozone has been lately eyed as a cause of degenerative diseases of the nervous system. It has even cracked auto tire rubber in our seacoast areas.

A negative ion generator is available either as a unit to fit into the ductwork of your warm-air heating system, or as a tabletop model for your living room. Negative ions are said to relieve hay fever symptoms, headaches, respiratory diseases. They are claimed to speed healings of burn wounds and to relieve pain. They relieve "stuffy" air in closed rooms, contribute to a feeling of well-being and alertness. Do you recall how charged with excitement the air seems to be just before a summer thunderstorm? At this time, the atmosphere has a superabundance of negative ions that are said to stimulate body glands and to increase the ability of the lungs to absorb oxygen. (For more information on negative ions, look for a story in the next issue of House Beautiful.)

If you're spray painting, power sanding, or driving your car down an exceedingly dusty or exhaust-filled road, there's a low cost (about $5) lightweight respirator mask you can wear. It covers only the nose and mouth, does not restrict vision, and does a good job of trapping particles even as small as cigarette smoke and organic vapors such as auto exhausts. It's even fairly good-looking, as respirators go.

Ultraviolet lights, proved highly effective against influenza, pneumonia, and other airborne bacteria, can be installed in the ductwork of your warm-air heating system, or as freestanding lights near ceiling height. Be sure to clean them regularly and to install them so rays can't reach eyes directly.

COMMUNITY ACTIVITIES

What can you do, besides reducing your own pollutions and keeping them at arm's length with mechanical gadgets?

You can act as an unofficial smoke observer. Your air-pollution control officer or health department will welcome your reports, since these departments are perennially understaffed.

If your city does not have an air-pollution control ordinance, you can start a citizens' committee to have one enacted. The SOS group (Women's Organization to Stamp Out Smog) of southern California numbers 60,000 and is growing larger every day.

Get your local merchants in on the act. Clean air is good business for them. It keeps downtown attractive, reduces spoilage of goods, and cuts window cleaning and other housekeeping costs.

You should actively support "Cleaner Air Week," which is a nationwide activity sponsored every October by the Air Pollution Control Association. The association, with headquarters at 4400 Fifth Avenue, Pittsburgh, Pa., can also supply you with technical information about air pollution.

As a last resort against flagrant sources of air pollution, you and your citizens' committee can invoke the nuisance laws on the statute books of nearly every State. Your city attorney can enforce these regulations.

Industry, however, is usually willing to clean itself up. Air-pollution abatement equipment is very costly, yet does not contribute in any way, in most cases, to reduced operating costs. One Pittsburgh steel company has just spent over $10 million for control equipment on their open hearth furnaces. Industry in the United States spends upward of $50 million annually for air-pollution control devices. Whatever you do, don't let your committee or club support hasty, ill-conceived air-pollution laws. Industry can't comply, and you won't solve any problems. Go at the problem calmly, enlist the services of the Air Pollution Control Association and your State health department.

HOW ST. LOUIS AND PITTSBURGH CLEANED UP THEIR SKIES

Credit for rolling back black canopies of smoke from these two cities goes to an aroused citizenry. Stirred up by angry women, action groups got behind an unremitting municipal drive to educate the people; to elect administrations pledged to clean up their towns; to get enough money appropriated to establish smoke-control bureaus, manned by professionals.

Tough ordinances were passed. They ordered every homeowner, business house, industrial plant, railroad locomotive, and river barge to use smokeless fuel, if heating equipment were fired by hand; to install a mechanical stoker, if local, soft smoky coal were burned.

Getting people to burn more expensive smokeless coal when each city is in the midst of a large soft coal-producing field makes this cleanup program, initiated by St. Louis, adopted by Pittsburgh, as dramatic as it has been successful. Pittsburgh has gone a step further to control additional pollutants, fumes, mists, dust, and odors, by installation of filters, electrostatic precipitators, and scrubbing equipment, and pollen, one of nature's contributors to our atmospheric plight, by using herbicide sprays on all city lots.

THE COST OF SMOKE CONTROL

Key to the success in both towns is in applying the law impartially. The division of smoke regulation in St. Louis (operating on a $110,000 budget and taking in around $100,000 in permit fees) and Pittsburgh's bureau of air pollution (with a $160,000 budget and $13,500 taken in fees) are empowered to enforce a strict ordinance. They can seal any heating equipment if violations are reported against it, an effective punitive measure. After 20 years of control in 1, 10 in the other city, both continue to police their skies with 10 to 12 field inspectors.

Such are the prices these towns had to pay for the cleanup job. No matter how high, medical and public health authorities warn that no price is too high for clean air.

Your health, and that of your children, need not be steadily undermined by air pollution, no matter how fast the population explodes, no matter how many new pollutants spew into the air.

By doing all in your power to reduce your own contributions to air pollution, by protecting yourself against existing air pollution, and by community activity to end others' pollutions, you can clean up the air. Some day Los Angelinos hope to see old Mount Baldy rear her head again through the murk and gloom of smog. Some day, airline pilots will be able to rely on safer visual flight upon arrival at our big cities. Some day chronic bronchitis and lung cancer may be as uncommon as smallpox. It is up to all of us.

Mr. FOGARTY. Mr. Denton?

BACKLOG OF UNFINANCED WASTE TREATMENT PROJECTS

Mr. DENTON Do you have any record as to the number of projects that are worth while and awaiting Federal allotment before they are built?

Mr. McCALLUM. As of February 28 there were 503 approved projects in the States in our regional offices that would require $41.1 million, and the States report an additional 888 projects that would require $75.2 million that are in preparation in municipalities or in the hands of the States but which the States have not yet approved and certified.

Mr. DENTON. That is, you need $75 million additional to complete everything that you have had in applications?

Mr. McCALLUM. Everything that has been reported by the States, being in the pipeline at this time, some of which has not yet reached the States, would require about $125 million; yes, sir.

Mr. DENTON. How much is there that should be built beyond what applications cover?

Mr. McCALLUM. We have had just a recent report by the States, that is, about the first of the year. They reported the need of 5,200 projects that would cost $2 billion.

Mr. DENTON. And in your plans, over how long a period do you propose to build them?

Mr. McCALLUM. Well, if we can increase our present rate of construction up to the level of $600 million a year, which we and the States have agreed would be necessary, it would be, hopefully, in good shape in about 10 years.

Mr. DENTON. I live on the Ohio River, and they have done very well, I think, on putting sewage disposals plants along the river. I think on the Indiana side there are only three communities on the river that don't have sewage disposal plants. And they are in the process of being built.

Do you know if that is right or not?

Mr. McCALLUM. I do think that is correct.

Mr. DENTON. Could you tell me how Kentucky is in that respect?

Mr. McCALLUM. I believe the larger communities on the Kentucky side have been taken care of. I am not sure about some of the smaller ones.

Mr. DENTON. But the need for this construction is greater than it was a year ago?

Mr. McCALLUM. Yes, I think that is correct. Our annual rate of expenditures is not keeping up with the growing problems—this is something like the highway problem—you may catch up in one place and lose a little ground somewhere else.

Mr. DENTON. For how long have you recommended the $100 million? The Blatnik bill was vetoed.

Mr. McCALLUM. We have not taken a position, to the best of my knowledge, our Department hasn't taken a position—Mr. Kelly says President Kennedy had recommended doubling the amount in the appropriations.

Mr. KELLY. That is in the national resources message that the President sent to Congress.

Mr. DENTON. Of course you couldn't pass an appropriation until you passed the legislation.

ENFORCEMENT POWERS OF THE POTOMAC RIVER BASIN COMMISSION

What have you done about the Potomac River Basin?

Mr. McCALLUM. We have an enforcement case on the Potomac River, sir. We had a conference 2 years ago last January, some fieldwork, and then a second session of the conference. We have the agreement between the District of Columbia, Maryland, and Virginia on a time schedule for corrective measures by the three jurisdictions, and by 1966 these measures that were agreed to at the conference should have been completed and implemented. And that will make a material difference in the Potomac.

Mr. DENTON. Bring me up to date on this. You know this committee makes an appropriation for the Interstate Commission on the Potomac River Basin; it is not very large, I think, $5,000 a year. But Maryland, Virginia, West Virginia, and Pennsylvania also contribute to it.

Now does it have any enforcement powers like the Ohio River Basin Commission does?

Mr. McCALLUM. No, sir; they do not.

Mr. DENTON. Has any legislation or anything been proposed to give them enforcement powers like the Ohio River Basin has?

Mr. McCALLUM. None of which I am aware.

ALTERNATIVE ENFORCEMENT POSSIBILITIES

Mr. DENTON. Do you think it is possible to do anything else unless you have that same authority that you have on the Ohio River Basin?

Mr. McCALLUM. Yes, Mr. Denton. I think it is. I am very much interested in this interstate commission work, and I think there are jobs for an interstate commission that haven't been real well gone into—forestry, civil defense, water resources, and probably many others. And my own conviction is that it is questionable whether they can go real far on the enforcement side. The Ohio River Valley Sanitation Commission has had only one case, and that was one where Ohio had had some difficulty with one of the communites over on the east side of the State.

Mr. DENTON. You mean on the Ohio River they have all complied with the directive?

Mr. McCALLUM. They have done it by getting the States together, better community relations, a better understanding of what each State is going to do. And I think it is agreed that they have really done a good job, it has been very well worth while.

Mr. DENTON. I think they have done an excellent job.

Mr. McCallum. Without enforcement.

Mr. Denton. But I understand that when the commission issued an order, the community had to comply with it.

Mr. McCallum. I believe they issued one to a West Virginia community, also, and they started an enforcement on one Ohio community, but they have done the majority of their work in another manner, that is, getting the States to do it.

Mr. Denton. The State commission—I can't give you the name of it offhand—issued an order to the community telling them to build a sewage disposal plant, and they went ahead and built it.

Mr. McCallum. Generally, States with enforcement authority have made some use of it. They find, however, that they get pretty good compliance without using it a great deal.

Mr. Denton. Don't you think we ought to have some similar provision on the Potomac?

Mr. McCallum. That would be up to the States. I think there has been much accomplished in the Potomac by the Potomac River Commission.

Mr. Denton. I think that is all.

Mr. Fogarty. Do you have anything else you want to say?

Mr. McCallum. I think not, sir.

RESEARCH GRANTS

Mr. Fogarty. Dr. Anderson, do you want to say anything in summary?

Dr. Anderson. Yes. I would like to touch on a point that you mentioned.

With regard to research grants, Mr. Chairman, the requests for the environmental health program activities provide for the expected continuation of the grants that are in existence this year, and for the same number of new grants as we had this year. This is the way that we are anticipating the growth of the research grants program.

In the development of this program by the Public Health Service, we are finding a great deal of interest on the part of universities, foundations, and various organizations that have talents and competence in research and training.

We look forward to a heightening of this interest in the years to come, and this forecasts, I believe, the development of additional technical knowledge which will speed the day of control of some of these pollution problems.

That is all I wanted to comment on.

Mr. Fogarty. Some of these universities would close up if it weren't for the Public Health Service grants, wouldn't they?

Dr. Anderson. Not in environmental health fields yet, sir.

Mr. Fogarty. I said Public Health Service. That covers a lot of territory.

Is there anything else you would like to say?

Dr. Anderson. No, sir.

(The following was subsequently submitted:)

RELATIONSHIP OF PHS ACTIVITIES TO ACTIVITIES OF OTHER AGENCIES

At several points in the hearings, in particular those parts dealing with environmental health programs, the question of duplication or overlap with the activities of other agencies of Government was raised. These instances include the respective relationship of our radiological health activities to those of the Atomic Energy Commission; of the occupational health program to the Bureau of Mines, Bureau of Labor Standards, and the Department of Agriculture; the respective relationship of the milk and food program to Department of Agriculture and the Food and Drug Administration; the relationship of our accident prevention program to the road and highway agencies, automobile and other industries; the relationship of the water pollution program to various agencies in the natural resources field.

The Public Health Service under the broad activities assigned to it by Public Law 410 has the basic mission of protecting the health of the people and in carrying out this role it must work with and through a number of other governmental agencies at the Federal, State, and local level. In the case of the air pollution and water supply and pollution control programs, Congress has passed legislation (Public Law 84–159 in the case of air and Public Law 84–660 in the case of water) assigning to the Public Health Service specific responsibilities in relationship to the prevention and control of pollution of these natural resources. I would like to make the point that the existence of these overlapping program relationships is not the result of confusion and duplicative bureaucratic competition but is rather a result of our carrying out our role as the protector of the public health in virtually every major field and more particularly the environmental problem areas. In these fields it is not our responsibility to do the entire job but to do that aspect relating to health. For example:

In occupational health our job is to see that the health hazards of mining are defined and are made known to those responsible for mine regulations. These include the Bureau of Mines, Bureau of Labor Standards, and numerous industry groups.

In the milk and food program we study various processes so that the best public health practices can be taken into the food and food service industries. Therefore, inevitably we work in conjunction with the regulatory agency (Food and Drug Administration) and industries concerned, such as dairy farming and shellfish producing and distributing operations.

In accident prevention our mission is to see that the health and safety aspects with which the accident prevention program is concerned are made known to and taken into account by those in a great variety of fields which have a bearing on the incidence of accidents. That is why our work touches on many agencies and institutions such as road and highway agencies, motor vehicle licensing authorities and automobile manufacturers, to name a few.

In the water field we are concerned with water pollution and water supply from the pollution standpoint. We work with others who have a stake in the water resource field also but whose primary concern is in flood control, navigation, conservation, or water power.

In the radiation field we do not seek to promote and control the utilization of atomic energy—that is the role of the AEC—our responsibility is the protection of the public health in these matters.

This, then, is an elemental and essential characteristic of the Public Health Service's mission and it requires that the Public Health Service move into fields where other interests have different responsibilitiees. We cannot abdicate our responsibilities for health protection because some other agency is also concerned with a general field.

Mr. FOGARTY. Dr. Terry, is there anything you would like to say before we conclude our hearings on environmental health?

Dr. TERRY. Nothing specifically.

USE OF AN ADDITIONAL $100 MILLION BY NIH

Mr. FOGARTY. I have one problem. I was asked by a radio man to answer a few questions at noontime about some of the advances made in heart and cancer. And one of the questions he asked me which I didn't expect was, "How much do you think we ought to be spending in the field of the Institutes of Health?"

And I told him we ought to be spending about $100 million more than the present budget calls for.

Do you think if we increased the President's budget by $100 million, that it could be spent in a wise and efficient manner?

Dr. TERRY. Yes, sir.

Mr. FOGARTY. Thank you.

Is there anything else before we close from any of the other people who have testified? We have covered quite a bit of territory in this one hearing, if you do have something else to add feel free to do so.

RECOMMENDATIONS OF THE PLUMBING CONTRACTORS

Mr. GILBERTSON. You asked a question last night as to whether we were familiar with a letter from the plumbing contractors and the National Association of Plumbing Contractors and whether we have a statement on it.

Mr. FOGARTY. Mr. Michel is also interested in this.

Mr. GILBERTSON. We do have a statement which we can supply for the record, if you wish. Mr. Michel mentioned it at the close of the hearings this morning. I see he is gone now.

Mr. FOGARTY. I am sure he wanted that question answered.

Do you have it?

Mr. GILBERTSON. Yes, sir, we can supply it.

Mr. FOGARTY. We will leave it with Mr. Michel and will place a copy in the record.

(The letter from the association and the comments of the Public Health Service follow:)

NATIONAL ASSOCIATION OF PLUMBING CONTRACTORS,
Washington, D.C., March 13, 1961.

Hon. JOHN E. FOGARTY,
House of Representatives,
Washington, D.C.

DEAR FOGARTY: The National Association of Plumbing Contractors has been intimately concerned with the work of the Public Health Service in the plumbing field. We have been privileged to serve as a member with other national organizations of the Public Health Service Technical Committee on Plumbing Standards. This committee has performed a vital function in revising the ASA A40.8 National Plumbing Code of the American Standards Association. The National Association of Plumbing Contractors takes considerable pride in the role it played in the original establishment of this committee and also is appreciative of your support, particularly at the time of the hearing with the U.S. Public Health Service on February 20, 1956, regarding plumbing codes.

It is becoming increasingly apparent that the scope of the Public Health Service activity in the plumbing field should be substantially broadened. The present level of expenditure to support the committee activity amounts to $5,000 per year. This low level of financial support has seriously handicapped the committee and the service in the revision of the code. More important, however, is the need to expand these activities to further a comprehensive program related to public health aspects of plumbing.

The direct relationship between faulty plumbing and disease has been firmly established over the years. A progressive program directed toward the establishment and application of reasonable standards on plumbing nationally is urgently needed. The committee activity referred to previously has identified areas in which research is needed. In common with other phases of building technology, new procedures and materials application require study to permit their inclusion in standards of practice. For example, little is known regarding the technical requirements needed to permit the use of plastic piping materials for water and waste lines. While industry does carry on certain related research pertinent to their specific interests, little is being done to improve the technology of plumbing from the standpoint of the ultimate consumer, namely, the house of property owner. It has been estimated by reliable authorities that between $50 to $100 per building unit might be saved on plumbing costs through application of new procedures and techniques. In simple terms, a comprehensive program of research, standards development, and application in plumbing is urgently needed to permit our industry to keep pace with other phases of the building industry and to provide the greatest benefit to the public.

The Public Health Service is ideally situated to undertaken such a program because of the health implications relationships to existing programs within the Service, and technical competency.

Based on our studies, it is recommended that an amount of $250,000 annually be appropriated for such a program. The suggested distribution and use of these funds could be as follows:

I. Headquarters direction, $25,000: This will cover the costs of administration and technical direction of the program, standards development, and related activities.

II. Research activities, $145,000: These activities would cover studies on hydraulics and pneumatics of plumbing systems, water conservation measures, venting and trapping, effects of detergents on drainage systems, corrosion phenomena, studies of new classes of materials having application to plumbing systems, and related studies.

III. Field operations, $80,000: This involves the assignment of one engineer to each regional office to provide technical assistance and consultation to State and local health and building agencies on cross-connection survey, standards promotion, training, and such field research studies as may be needed to develop data on suitability of criteria under field conditions.

In view of the economic implications to the economy, the benefit to the public, and assistance to the plumbing industry generally, it is hoped that your committee may look with favor on this request. May I assure you of the complete support of this association in the accomplishment of the program with its ultimate goal of health protection and an improved standard of living.

Cordially,

Carl N. Finley, *President.*

Proposed Public Health Service Plumbing Program

The Public Health Service has a continuing role and responsibility in the public health aspects of plumbing systems. The relationship between faulty plumbing and disease transmission has been dramatically demonstrated on numerous occasions. It is vital to the protection of the public health that basic principles be observed in the installation and operation of plumbing systems to break this chain of disease transmission. Water supplies must be protected against the hazards of backflow (backsiphonage) and cross connections whereby contamination might be introduced into the supply. In addition, certain aspects of the drainage system must be properly designed and constructed to prevent the creation of health hazards.

The Service has a further legal responsibility related to plumbing under the provisions of the interstate quarantine regulations which require the certification (approval) of water supplies used by interstate carriers. This certification involves a consideration of the public health aspects of the system from the source to "the free flowing outlet of the ultimate consumer." The health hazards in plumbing systems served by the water supply must of necessity be considered in the overall certification.

ACTIVITIES

The Public Health Service has historically participated in development of plumbing standards as carried on by various Federal and national organizations. These standards have been developed to serve as criteria to Federal agencies concerned with plumbing installations and as guides to State and local jurisdictions charged with the responsibility of supervising plumbing. Most State and many local health departments are charged with such responsibility. As a result, the Service has given technical advice and consultation on request to these agencies in the development of reasonable and adequate standards.

To assist in the discharge of its responsibilities in this area, the Service has established a Technical Committee on Plumbing Standards. This Committee has provided invaluable service within the limits of resources in giving guidance on recommended changes based on technological developments in the field of plumbing. The work of the Committee has been seriously handicapped by the lack of resources to carry on needed research and through lack of a Service program directed toward the promotion and updating of outmoded standards on a national basis. The level of expenditures for this activity has approximated $5,000 per year over the past 5 years.

The health and economic benefits resulting from uniformity and public health protection in plumbing codes is difficult to evaluate. For example, the reduction of inventories, simplified installation practices, and elimination of unnecessary requirements will result in savings to the manufacturers, installers, and purchasers of plumbing. It has been estimated that such savings may amount to some $50 to $100 on the average residential installation.

It has been proven by the Prestonsburg, Ky., study that the provision of adequate plumbing, primarily the provision of water under pressure in the home, dramatically reduces enteric disease rates in a community. Water conservation is assuming increasing importance and is in part achieved by the provision and maintenance of modern plumbing fixtures. An example of this is shown by the following illustration. A defective faucet or valve wastes 15 gallons of water in 24 hours. It is estimated that in the average household there is often at least one such condition, frequently in a toilet tank with a faulty float valve. Only constant surveillance and installing new washers or equipment can prevent this. In an average size community of 25,000 population there are 6,000 service connections. Thus, faulty plumbing can cause in such a community a daily waste of 90,000 gallons of water, enough to supply 1,800 persons at the rate of 50 gallons per captita per day, the average American per person water use.

The high development of plumbing in America and its use by the people has been the result of at least three factors. First, the advances in plumbing fixture design and manufacture achieved by the industry. Second, the improvement of techniques of installing plumbing by plumbers and plumbing contractors. Third, the requirement by health agencies that basic plumbing be installed for the protection of public health.

Concurrently with the advances of plumbing technology, but unfortunately at a much slower pace, has been the development and application of plumbing codes.

However, in recent years, for various reasons, plumbing research has practically ceased. This in spite of the fact that modern plumbing practice has often demonstrated the lack of scientific evidence to support or explain certain observed plumbing phenomena. An example is water distribution system sizing. Nearly all such design is presently predicated on factors developed 30 years ago, factors which were then assumed to apply universally, that is regardless of the type of occupancy of a building. In other words, a school, factory, and apartment, were all treated alike. It is now known that this assumption does not hold true and that overdesigning and its attendent waste of pipe and water is resulting. The entire procedure needs to be reinvestigated and the present salient factors determined.

In order, therefore, for the United States to continue its leadership in the plumbing field, there is an immediate need for stepping up plumbing research and also for the promulgation of adopting and enforcing better plumbing codes.

It is evident that a matter which is so vital to the health and economic welfare of the American people should receive guidance and recognition at the Federal level. Of the governmental agencies most concerned and currently active in the field none is so appropriate to conduct such work as the Public Health Service. This agency is also undergoing reorganization under which there will be increasing attention to all facets of the environment of man, including plumbing.

A PUBLIC HEALTH SERVICE PLUMBING PROGRAM

The nucleus for an expanded plumbing program exists in the Public Health Service through the Technical Committee on Plumbing Standards and the PHS staff which has been working with the committee. Through established relationships with State and local health agencies, avenues are open for the active promotion of improved plumbing programs throughout the Nation.

RESEARCH

There is need for research and investigation into the broad area of plumbing and water conservation. Designs of plumbing fixtures such as toilet flush tanks and valves are needed to cut back on water use. Water saving devices for faucets need to be developed. Part of this research involves determination from a health standpoint, of minimum quantities of water required for flushing toilets and urinals.

Basic and applied research programs are needed in the area of cross-connection control. Outbreaks of disease continue to occur from potable water which has been contaminated through a pipe cross connection with impure water or substance. More effective, efficient, and economic backflow protecting devices need to be developed.

Substantial research is needed on the hydraulics and pneumatics of plumbing systems. The use of new materials for piping, changing nature and composition of wastes, and related factors require study to establish loading limits.

STANDARDS PROMOTION

The National Association of Plumbing Contractors believes that there is great need to promote the adoption of modern plumbing codes. This is evidenced in that of the 23,000 U.S. municipalities provided with public water supplies, only a fraction are using up-to-date modern, plumbing codes. The Public Health Service is a logical focus activity in the area by virtue of having developed the draft document of the code and by virtue of its having representatives in eight geographical locations across the Nation. This activity would be closely coordinated with the Service activities on the certification of water supplies.

ORGANIZATION OF A PLUMBING PROGRAM IN THE PUBLIC HEALTH SERVICE

To accomplish the objectives and satisfy the needs described above, it is proposed to establish with the Public Health Service an organization of the divisions and estimated cost given as follows:

Administrative divisions:		*Estimated cost*
Headquarters direction		$25,000
Field operations, 8 regional offices		80,000
Research		145,000
Personnel	$75,000	
Facilities, equipment, and supplies	70,000	
Total		250,000

SUMMARY

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STATEMENT ON PUBLIC HEALTH SERVICE INTEREST AND ACTIVITIES IN PLUMBING

PLUMBING AND DISEASE

The spread of gastrointestinal infectious diseases because of unsafe plumbing has been dramatically proven both in the laboratory and in the field. The classical outbreak of this type occurred at the World's Fair in Chicago in 1933. Contamination was introduced into the potable water systems of hotel buildings through faulty plumbing installations which resulted in an outbreak of 1,400 cases of amoebic dysentery, including 98 deaths.

More recent examples include an outbreak of undulant fever in 1938 at Michigan State College caused by a cross-connection with an aspirator in a laboratory sink which drew disease organisms into the water system through back siphonage. Eighty cases and one death resulted. In 1942, an outbreak of bacillary dysentery at Newton, Kans., was traced to sewage entering the water system from frost-proof toilets and hydrants. At least 2,500 cases resulted. In Atlanta, Ga., in 1959, body fluids from a mortuary table were siphoned into the potable water supply of a funeral home. In fact, several Federal buildings located in the Washington area have had difficulties through backflow of boiler treatment and anticorrosion compounds into the water supply systems. Prohibition by the Public Health Service of the interstate carrier water supply at Hoboken, N.J., in 1960, because of gross contamination of the potable water attributed to backflow connections on the system, was avoided only by prompt emergency chlorination of the supply.

It has been demonstrated both in the field and in the laboratory that vacuums may occur in the water distribution system of a building. Under such vacuum conditions it is obvious that contamination from the drainage system or plumbing fixtures can easily be drawn into the drinking water supply system. In general, plumbing defects having public health implications may be divided into the three following groups: (1) Direct or indirect connection of the water supply system to pipes, tanks, or plumbing fixtures containing sewage, waste water, or other foreign material, through which such material might be siphoned, forced, drained, or otherwise introduced into the water supply system; (2) any connection which would permit the contamination of food, drink, or utensils used for the preparation or serving of foods, and (3) any condition which would permit the contamination of surgical equipment such as instruments, bandages, sterile water, etc. (these situations prevail all too frequently in hospital plumbing systems).

A further consideration regarding plumbing and public health is the availability of plumbing within the house. Conclusive data has been obtained by the Public Health Service as a result of the Prestonsburg, Ky., study which showed that enteric disease rates can be substantially reduced through the provision of modern plumbing facilities within the home. The evidence clearly points out that the provision of running water within the residence, the installation of adequate toilet facilities and modern plumbing for personal hygiene results in substantial reduction of enteric diseases. These data have been useful to State and local health agencies in providing definite evidence that plumbing facilities bear a direct relationship to health.

CURRENT ACTIVITIES

The Public Health Service has a vital and continuing interest in the public-health aspects of plumbing. The Service is continuing to furnish staff services for the activities of a technical committee on plumbing standards which is currently engaged in a project on revision of plumbing standards. The membership of the committee includes representation from various national organizations interested in development of reasonable and adequate standards for plumbing systems.

Many State and local health departments, as well as housing and building officials, are charged with the responsibility for supervision of plumbing installations. These groups frequently request technical assistance from the Public Health Service in connection with plumbing standards and in particular the administration of their respective programs. Insofar as possible, the Public Health Service attempts to provide assistance as requested. The present level of activities amounts to about $5,000 per year.

RELATIONSHIP OF PLUMBING TO VARIOUS HEALTH PROGRAMS

Many categorical programs of the Public Health Service involve consideration of the public-health aspects of plumbing. An important facet of the water supply certification program for interstate carrier water use is the adequacy of plumbing regulatory control by local jurisdictions. The safety of a public water supply system cannot be evaluated without checking on the potential hazards associated with plumbing connected to such systems. It should be noted that under the water supply certification program, the Public Health Service exercises surveillance over municipal water supplies serving about 70 percent of the U.S. population.

The hospital construction program is deeply concerned with the protection provided by plumbing within medical facilities. The standards development group referred to above is developing criteria for plumbing for hospital facilities. In our restaurant sanitation program, sanitary plumbing is an important element and this point has been recognized in the recommended code prepared by the Public Health Service covering restaurant sanitation. This same situation is equally true in connection with milk processing, both on the farm and in the pasteurization plant.

EXISTING AND FUTURE NEEDS

The foregoing résumé highlights in certain respects, the existing and future needs in this field. In general, the approaches which have proven successful in connection with development of other public health programs would be useful in the development and application of health knowledge relating to plumbing problems. Future activities may be broken down into the following three categories:

1. *Research and standards development.*—As a result of the activities of our technical committee on plumbing standards, various problems requiring further research and study have been highlighted on which study is needed for adequate standards. It is recognized that improvements in standards of living and the concurrent improvements in plumbing continue to raise questions for which there are no ready answers. Today, for example, plumbing systems have to be designed to service new types of appliances not in common use a few years ago. Such appliances as automatic-cycle clothes-washing machines, dishwashers, water-cooled air-conditioning systems, garbage grinders, and similar devices require the development of criteria in order to permit rational design of water distribution systems. Criteria applicable to drainage systems are subject to serious question. Because of foam production, new detergents are having a serious effect on the ability of drainage systems to promptly carry away the waste from fixtures particularly in multiple-family structures.

Within industry, tremendously increased quantities of water are being used. The problems of cross connection and back siphonage within industrial establishments are serious. Due to changes in patterns of occupation, living and recreation, a critical review is needed on certain existing standards on fixture schedules currently in use on a national basis. The Service would initiate studies in the several areas of research where basic information is needed and upon completion of such studies would translate the findings into standards suitable for adoption and enforcement by local jurisdictions.

2. *Field studies and operations.*—The Service is receiving increasing numbers of requests from State and local health agencies for assistance in conducting cross-connection and backflow surveys, a problem which was highlighted in a technical paper presented at the last meeting of the American Public Health Association. Such studies also are essential in our program on certification of carrier water supplies. There is also a need for the Service and the health departments to observe in the field the result of certain practices, that have public health significance, in connection with the design and installation of plumbing systems. Such activities would be most helpful in orienting responsible officials in the details of a public health plumbing program.

3. *Training.*—Training is necessary in order to disseminate results of research and to reduce the timelag in the application of new knowledge. With the continuing turnover of personnel in the field, the increased numbers of people concerned with the problem and the advent of new developments which are being introduced into the field of plumbing, a continuing, active program of training is essential.

FISCAL REQUIREMENTS

The described program could be initiated during fiscal year 1962. Complete development should be phased out over a 3-year period. A portion of the first year would be required for the acquisition of necessary equipment and other facilities needed for the research aspect of the program. In addition, recruitment of qualified personnel would have to be phased out over the first 18 to 24 months of operation of such a program. In the light of these considerations, it is anticipated that the fiscal requirements for such a program would amount to:

Fiscal year 1962	$200, 000
Fiscal year 1963	250, 000
Fiscal year 1964	300, 000

In subsequent years, it is anticipated that expenditures would be distributed about equally between: (*a*) Research and standards development, and (*b*) field studies, operation, and training.

RECOMMENDATIONS OF THE APWA ON WASTE COLLECTION AND DISPOSAL

Mr. FOGARTY. I have another letter here from the American Public Works Association. It says that:

> The American Public Works Association has asked the Public Health Service to initiate a broad program of basic and applied research on refuse collection and disposal problems similar to those that have been developed in allied fields of activity.

Has this been brought to anybody's attention?

Dr. ANDERSON. Mr. Gilbertson can answer that.

Mr. FOGARTY. Are you familiar with this organization, and this letter?

Mr. GILBERTSON. Not with the letter, sir, but with their resolution.

Mr. FOGARTY. We will put the whole thing in the record.

(The letter referred to follows:)

AMERICAN PUBLIC WORKS ASSOCIATION,
Chicago, Ill., March 16, 1961.

HON. JOHN E. FOGARTY,
House of Representatives,
Washington, D.C.

DEAR CONGRESSMAN FOGARTY: It is my understanding that the Public Health Service has made provision in its budget request for the 1962 fiscal year for additional funds to expand its activities in the field of solid-wastes collection and disposal.

Since your committee will soon be giving consideration to this matter, I thought you would be interested in the enclosed resolution which expresses the views of the engineers and administrators throughout the country who are directly concerned with refuse collection and disposal problems.

You will note that this resolution was adopted by the membership of the American Public Works Association at its last annual meeting in New York City, August 15, 1960. It points up the importance of this subject to the American people and requests the Public Health Service to undertake a broad program of basic and applied research in this field.

The American Public Works Association is a nonprofit organization dedicated to the promotion of improved practices in the field of public works engineering and administration. A brochure about the association and a copy of its 1960 report to the membership is enclosed herewith to help acquaint you with the work of this organization. You will note that it is composed of over 5,000 public officials—most of whom are employed by local units of government who are engaged in refuse collection and disposal operations.

This association has, for many years, conducted a program of activities designed to assist municipal officials in their efforts to develop efficient methods of collecting and disposing of solid wastes. It has, for example, issued an authoritative text on refuse collection practice and will soon release a new 400-page manual on "Municipal Refuse Disposal." Unfortunately, it is not in a position to undertake the kind of research program needed in this field.

Therefore, the American Public Works Association has asked the Public Health Service to initiate a broad program of basic and applied research on refuse collection and disposal problems similar to those that have been developed in allied fields of activity. We sincerely hope that sufficient funds will be made available to the Public Health Service to enable it to initiate such a program.

Sincerely yours,

ROBERT D. BUGHER, *Executive Director.*

RESOLUTION RE ESTABLISHMENT OF RESEARCH PROGRAM IN FIELD OF SOLID WASTE COLLECTION AND DISPOSAL

Whereas the proper storage, collection, and disposal of community solid wastes is basic to a clean and healthful environment; and

Whereas the problems associated with solid waste disposal are becoming increasingly difficult and expensive to solve because of the adoption of more rigid air, land, and water pollution control requirements; and

Whereas improper disposal of community solid wastes can be a costly blight on the adjoining property; and

Whereas the expansion of our population and our growing metropolitan complexes will intensify the problems of disposal; and

Whereas the cost of collection and disposal of community solid wastes is one of the substantial financial burdens of our municipalities amounting to about $1,500 million, annually; and

Whereas there is an immediate need for a program of basic and applied research to stimulate progress and the application of technology in this field; and

Whereas the Department of Health, Education, and Welfare has excellent personnel and facilities available for the development of research programs effecting a healthful environment for the people: Therefore be it

Resolved, That the Department of Health, Education, and Welfare be requested to initiate action to establish a broad program of basic and applied research in the field of municipal solid waste collection and disposal.

Adopted by membership of the American Public Works Association at its annual business meeting in New York, N.Y., August 15, 1960.

Certified a true copy:

ROBERT D. BUGHER, *Executive Director*.

Mr. FOGARTY. What do you think of it?

Mr. GILBERTSON. Well, sir, we have an item, a very small one, in our program for 1962 which relates to the problem that APWA mentioned. As I recall, I think we provided for an increase of $9,000 and one position.

Mr. FOGARTY. That isn't going to solve the problem, is it?

Mr. GILBERTSON. I am afraid not.

Mr. FOGARTY. What do you think it would take to do a good job on this particular problem?

Mr. GILBERTSON. There was a well-developed preliminary plan for a program that combined research and technical assistance to the States which included about 10 positions and about $100,000 a year.

HISTORY OF 1962 BUDGET REQUESTS

Mr. FOGARTY. I think I asked every one of these agencies what they originally asked for, and then what the Department asked the Bureau of the Budget for, and what you were allowed. So if I missed any, you supply it for the record. I don't think I asked you, Mr. McCallum.

Mr. MCCALLUM. No, sir.

Mr. FOGARTY. Will you supply that for the record? And if I missed any others, will they supply it for the record?

Thank you very much.

(The requested data follows:)

HISTORY OF APPROPRIATION REQUESTED FOR WATER SUPPLY AND POLLUTION CONTROL AND GRANTS FOR WASTE TREATMENT WORKS CONSTRUCTIONS, FISCAL YEAR 1962

	Request to Department (1)	Request to Bureau of Budget (2)	Bureau of Budget allowance (3)	Change between cols. 3 and 1 (4)	Explanation of change	
Water supply and pollution control:						
Grants to States and interstate agencies	$3,000,000	$3,000,000	$3,000,000	0		
Research grants	2,670,000	2,670,000	2,670,000	0		
Subtotal grants	5,670,000	5,670,000	5,670,000	0		
Comprehensive programs for water pollution control	5,187,500	4,137,000	2,495,000	−$2,692,500	Great Lakes-Illinois Waterway	$1,100,000
					Chesapeake Bay	260,000
					Appalachian mine drainage project	180,000
					Upper Ohio River Basin	200,000
					Delaware River Basin	180,000
					Columbia River Basin	176,500
					Lower Ark-Red River Basin	77,000
					Lower Mississippi River Basin	180,000
					Southeast River Basins	170,000
					Lower Missouri River Basin	165,000
					Basic program	4,000
Enforcement of interstate water pollution control	2,176,000	1,790,000	1,647,000	−529,000	Federal installations	156,000
					General program-reconnaissance	373,000
Research	2,811,500	2,275,000	1,923,000	−888,500	Advanced waste treatment	473,500
					Toxocological surveillance	300,000
					Conventional waste studies	81,400
					Water-treatment conservation	33,600
Collection analysis and dissemination of basic data	1,200,500	1,190,000	1,138,000	−62,500	National water quality network	37,000
					Inventory of waste treatment facilities	25,500
Technical services	2,486,500	2,160,000	2,155,000	−331,500	Special problems of waste treatment	331,500
Subtotal, operations	13,862,000	11,552,000	9,358,000	−4,504,000	Total	4,504,000
Total, water supply and pollution control	19,532,000	17,222,000	15,028,000	−4,504,000		
Grants for waste treatment works construction	50,000,000	47,500,000	50,000,000	0		

HISTORY OF BUDGET REQUEST FOR MILK, FOOD, INTERSTATE AND COMMUNITY SANITATION

Activity	1961 base	Surgeon General allowance	Department allowance	Bureau of Budget allowance
Research grants	$2, 548, 000	$3, 310, 000	$3, 310, 000	$3, 310, 000
Review and approval	60, 000	80, 000	80, 000	80, 000
Milk and food	1, 070, 300	1. 478, 600	1, 223, 000	1, 190, 800
Milk sanitation	508, 800	735, 000	590, 000	579, 000
Shellfish sanitation	309, 000	345, 600	345, 000	322, 900
Food-service sanitation	252, 500	398, 000	288, 000	288, 900
Interstate and community sanitation	806, 700	1, 182, 400	1, 045, 000	897, 200
Interstate carrier	593, 800	830, 500	773, 000	641, 740
General engineering	212, 900	351, 900	272, 000	255, 460
Training	62, 100	163, 000	126, 000	126, 000
Total	4, 547. 100	6, 214, 000	5, 784, 000	5, 604, 000

HIGHLIGHTS OF PROGRESS IN ENVIRONMENTAL HEALTH

Mr. FOGARTY. We will also place in the record the special progress report that you have prepared for the committee.

(The report referred to follows:)

HIGHLIGHTS OF PROGRESS IN ENVIRONMENTAL HEALTH

I. AIR POLLUTION

Within the past year, highlights in the work of the air pollution program are:

The passage of Public Law 86–493 has accelerated research related to the effects of motor vehicle emissions on human health. Significant program attention was given to the design and implementation of research projects needed to provide information in the required report. Included in these projects are: the field study of lead levels in community atmospheres; eye irritation studies; levels of gaseous pollutants found in auto exhaust, in community atmospheres; and short-, intermediate-, and long-range exposure of experimental animals to irradiated and nonirradiated auto exhaust.

The auto exhaust test facility at the Sanitary Engineering Center was used in determining certain criteria for the design of animal exposure facilities to be used in the accelerated research program. At this test facility, work also continued on the short-term exposure of vegetation and animals to auto exhaust and on the relationship of emissions to engine condition. Samples of raw auto exhausts are being collected under all engine-operating conditions for use in the establishment of gross carcinogen levels in the exhaust emissions and in the development of road-sampling equipment to be used in a comprehensive study.

At Wayne State University, support is being given to a study of the life characteristics of separate animal colonies exposed to urban air pollution, to pollution arising from a heavy concentration of automobiles, and to highly filtered urban air. A similar study is being planned in Los Angeles.

The previously developed analytical method for 3.4-benzpyrene, a potential carcinogen, was applied to air samples from 103 cities and 28 nonurban sites in the United States. The compound was detected in all areas, with the highest levels occurring in the eastern and midwesteern sections of the country. The geometric mean of levels in the cities was 16 times that of levels in nonurban areas. Nine of the cities were sampled and studied more intensively; although benzpyrene was present in only one of the fractionated samples taken in these cities, all fractions did produce tumors in animals. Work has been initiated, therefore. in the development of analytical methods for other organic compounds, particularly those polyaromatic and long-chain aliphatic compounds known to be carcinogenic.

A start has been made in adding 24-hour sampling for gaseous pollutants to the national air-sampling network. Three gases are being sampled in a limited number of cities; the development of sampling techniques for two additional gases is underway.

A forecasting service for the prediction of prolonged periods of high-air-pollution potential was initiated for the entire area east of the Rocky Mountains. Stagnation forecasts are received by certain Weather Bureau offices who are prepared to accept requests for these forecasts from governmental and private organizations. Already, 82 governmental agencies, industries, and universities have indicated a desire to receive notification of the forecasts.

With Public Health Service support, the School of Medicine of Tulane University initiated a study of the key factors associated with episodic asthma attacks in New Orleans. Now that it is possible to predict many of these attacks, extensive effort is directed toward a determination of the specific air pollutant, or pollutants, implicated and of the specific source from which they emanate.

With Public Health Service support, the Armour Research Foundation is studying the combined exposure of experimental animals to ozone and bacteria. Preliminary results of this study indicate that the presence of ozone in the atmosphere enhances the incidence of respiratory infection.

Through research grants, studies were initiated, or continued, in 1961 on many aspects of the air-pollution problem. Approximately $1½ million in research grant funds were awarded.

Eight grants were made to universities for continuation of their air-pollution curriculums. These curriculums are developing very satisfactorily. Five training grants were awarded to five individuals from program funds.

On request, statewide appraisals of air-pollution problems in Minnesota, Pennsylvania, and Florida were completed; the report of a similar appraisal in North Carolina was released. The air-pollution problems in Hamilton, Ohio; Charleston, S.C.; Lynchburg, Va.; and Washington, D.C., were evaluated.

Consultation was provided to a number of State and local agencies and to industry, on the nature, causes, extent, effects, and control of air pollution. The large number of such requests, in addition to the large number of communications from individuals seeking information, are indicative of an increasing interest and awareness in air pollution.

Results of an extensive technical study in the Detroit-Windsor area were published in cooperation with the International Joint Commission. Recommendations were prepared for the control of air pollution from vessels plying the international waterway at Detroit.

Training in air pollution was provided to 150 persons in 9 courses, covering 8 technical subject areas, at the Sanitary Engineering Center. A 2-day orientation course was presented in 3 cities, with a total attendance of 289. Trainees were from all levels of Government, from industry, and from universities.

The Public Health Service published the report, "National Goals in Air Pollution Research," which identifies goals for the next decade and recommends levels of effort to meet these goals. The report was developed by an expert group of consultants from outside the Federal Government.

In September 1960 the Division of Air Pollution was created to provide for greater focus of activities, both within and outside the Public Health Service, and to enhance a more comprehensive, interdisciplinary approach in research, technical assistance, and training.

II. MILK, FOOD, INTERSTATE, AND COMMUNITY SANITATION

1. *Research grants*

In fiscal year 1961, the number of research grants awarded increased to 208 from 63 in 1960.

Past experience suggests that some 415 applications for new and continuation grants will be received in 1962 and that some 265 will be approved for funding.

2. *Milk, shellfish, and food-service activities*

Substantial progress has been made in implementing congressional directives of 1960 and 1961 for increased emphasis on Public Health Service activities concerned with milk, shellfish, and food-service sanitation activities. Service activities have been reoriented to strengthen the research phase of the program and to maintain the cooperative interstate milk and shellfish activities at less hazardous levels.

With the increase of $230,000 in 1961, research has been initiated, and current studies expanded, to:

(*a*) Determine the influence of present-day methods of bulk handling, processing, and long-distance transport on the growth of various forms of bacteria found in milk.

(*b*) Determine the precise temperatures and times required for the thermal destruction of pathogenic micro-organisms by processes which utilize higher temperatures and shorter holding periods than those now used in conventional methods of pasteurization.

(*c*) Determine common types and sources of toxigenic staphylococci occurring in milk and milk products.

(*d*) Develop simplified procedures for identification of chlorinated hydrocarbon insecticides in milk and determine quantitative levels.

(*e*) Develop rapid and reliable tests for the detection of a variety of chemical and biological pollutants in shellfish and shellfish growing waters.

(*f*) Study aquatic environmental factors which influence the contamination and purification of shellfish.

(*g*) Determine factors affecting the growth and metabolic activities of staphylococci, salmonella, and other pathogenic micro-organisms in those foods most frequently involved in disease outbreaks.

Other program highlights.—The cooperative State-Public Health Service program for certification of interstate milk shippers continued to increase; Public Health Service list published on January 1, 1961, includes 745 shippers located in 36 States and the District of Columbia.

Number of check ratings of interstate milk shippers has been increased from 260 in 1960 to approximately 350 in 1961. This requires the inspection of approximately 4,000 dairy farms and approximately 450 receiving stations and plants. The sanitary quality of milk has been maintained at a high level as indicated by the following mean ratings: raw milk for pasteurization, 92.83 percent; pasteurized milk, 94.13 percent.

During the past year, 38 State milk sanitation rating officers were certified by Public Health Service.

During 1961, Public Health Service will evaluate shellfish sanitation programs of 16 States and make approximately 400 plant inspections, as contrasted to 8 State program evaluations and 225 plant inspections in 1960.

The average State shellfish sanitary rating for all State programs was 88.3 percent as compared to 86.9 percent for the preceding year.

The Public Health Service list of certified shellfish shippers included approximately 1,600 shippers certified by participating States; an additional 61 shippers were certified by the Canadian Department of National Health and Welfare.

Considerable progress has been made on revision of the 1943 edition of the Public Health Service recommended "Ordinance and Code Regulating Eating and Drinking Establishments." It is anticipated that a prepublication draft of the new food-service sanitation manual will be ready for final review by the end of 1961.

3. *Interstate carrier and general engineering*

As a result of the increased resources in this field, it has been possible to reestablish a cooperative working relationship with State health agencies in the supervision of the quality of the finished water supplies serving interstate carriers. Approximately 175 joint surveys of these supplies have been initiated in cooperation with the State health departments and the waterworks officials in developing basic data on trace exotic elements or constituents in the supplies. This is being coordinated with a further study on quality control procedures in order to evaluate the effectiveness of currently acceptable treatment methods as compared to the changing character of raw water supplies. Cooperative relationships have been established with the National Heart Institute and the Communicable Disease Center in the development of studies relating to cardiovascular disease and infectious hepatitis.

The levels of inspection in connection with the interstate carrier activities have been increased. The vessel program is now being carried forward on the basis of annual inspection of the 2,207 vessels under surveillance, and semiannual inspection of the approximately 1,300 dining cars. The other phases of this program have been reoriented in the light of additional resources.

The Great Lakes study is developing information on pollution of the Great Lakes resulting from vessel operations, both interstate and foreign. Delimiting action has been taken by the Public Health Service to protect water supply intakes serving a population of over 5 million people on the Great Lakes. Studies are currently underway in connection with the development of criteria for sewage treatment units to be developed for vessels, surveys of water supply quality aboard vessels, preparation of criteria and units suitable for sewage treatment, and the preparation of a manual on port sanitation.

Cooperative studies of environmental health problems on a metropolitan basis have been undertaken, notably in the Fort Wayne, Ind., and Omaha, Nebr., metropolitan areas. These areas have been utilized to determine the suitability of a sanitation evaluation system useful to both professional and lay groups in evaluating their environmental health position and assisting in the development of an organized approach to their needs. Based on requests which have been received, it is apparent that substantial additional resources will be needed in order to permit the Public Health Service to provide the technical assistance, consultation, and research necessary to establish an active and progressive program in this field.

Training.—Approximately 200 persons will participate in training courses at the Robert A. Taft Sanitary Engineering Center. Assistance is being given in the planning and conduct of a seminar on environmental health and urban planning in cooperation with the Northwestern University. Over 300 participants are anticipated in 1962.

III. OCCUPATIONAL HEALTH

1. *Study of silicosis*

Since the environmental study of silicosis in metal mines being conducted by the U.S. Bureau of Mines was expanded to include medical studies, examinations have been completed of 8,800 employees of metal mines of 32 different types and sizes in 12 Western States. These studies consist of chest X-rays, occupational histories, medical histories, and tests of lung function. It is anticipated that a total of 15,000 miners and 75 mines will be included in this study, which has moved into midwestern and eastern mines. Results will be available in late 1961.

2. *Uranium miners*

Studies of the hazards of uranium mining have continued in collaboration with the National Cancer Institute, the U.S. Bureau of Mines, the Atomic Energy Commission, and the States. It has been shown that an excessive number of deaths are occurring due to lung cancer and to complications of silicosis. Because of this problem, a conference was held with representatives of the Federal Government and the Governors and other officials of the States concerned. Accelerated efforts were called for to complete definitive examinations on all uranium miners and to spur dilatory compliance with recommended measures to control radiation exposures in the mines.

3. *Toxicologic studies*

Studies were begun on how certain types of toxic substances found in the industrial atmosphere seem to neutralize the effects of other toxic compounds; the toxicity of oil mists; how industrial chemicals act on protein films as a mechanism model of lung injury; and changes in biochemical profiles of man and animals occurring as a result of exposure to chemicals. Other research has included the mechanisms of the pulmonary effects of oxidant gases, pharmacologic mechanisms of protection against oxidant toxicity, and immunochemical relationships of industrial allergens.

4. *Habitability studies*

The Division participated with the U.S. Navy in conducting habitability studies on board nuclear submarines. Air sampling devices for gases, dusts, and ion concentrations were used to determine the effectiveness of the air purification systems during submergence of the vessels.

5. *Animal feed mill study*

A study of the animal feed industry was initiated to determine any potential occupational hazards arising from the increasing use of additives as nutrition-boosters and disease-resistant agents. This study was dictated by concern that proper industrial hygiene control measures are being observed in the use of more than 50 additives, some of which could have serious effects. Chemical and biological assays of air samples and of urine samples are being carried out.

6. Training

Sixteen training courses and 12 seminars were presented in the field of industrial hygiene and chemistry. These were attended by more than 1,400 persons from State and local health departments, the armed services, and industry.

7. Consultative services to State and local health departments

Examinations were made of 302 celery farm employees following dermatitis outbreaks in Michigan. Over one-half displayed various stages of vesicular and bullous dermatitis on exposed areas along with depigmentation and hyperpigmentation from previous lesions. The dermatitis was shown to be a photoxic reaction to celery infected with pink rot fungus.

8. International abstracting service

Cooperating with the International Occupational Safety and Health Information Centre (CIS) established by the International Labor Organization, the Division of Occupational Health was designated the national center responsible for obtaining abstracts of U.S. literature in the occupational health field. Through the CIS the exchange of occupational health information on an international basis has been markedly improved.

IV. RADIOLOGICAL HEALTH

1. Research activities

Environmental exposures.—A study of the body burdens of radioactivity in the general population in the San Juan Basin area is underway. A laboratory has been set up in cooperation with the New Mexico State Health Department and we are currently establishing procedures in methodology for processing of food and excreta samples. Bone specimens are being gathered from the local area for deposition analysis. A sample population, meeting the 10-year residence requirement, has been selected and interviewed.

In St. Louis we are currently in the initial phase of studying the animal husbandry variables among the farms in several of the milksheds that have yielded different levels of strontium 90. Methods have been developed for collection, storage, and analysis of water, milk, feed, precipitation, soil, and vegetation samples involving the introduction of radionuclides into milk.

Medical exposure assessment.—The pilot phase has been completed on a study of X-ray exposure during pregnancy. The results indicated that "It seems quite feasible to collect information * * * on the frequency of radiological examinations during pregnancy." We are currently planning a nationwide study for a significant population.

In cooperation with Tulane University and New York University, a study is being conducted on population exposure resulting from medical use of ionizing radiation specifically geared to the per capita dose to gonads and various other critical organs. Pilot studies are currently being conducted with medical practitioners in those areas.

In cooperation with Johns Hopkins University, a manual is being developed which will serve as a guide to radiologists and X-ray technicians to minimize exposure to patients while maintaining the maximum quality of the radiograph.

Occupational exposures.—A study to determine the dose effect relationship among employees working around the reactor is underway in conjunction with the University of Pittsburgh. The first phase involving the securing and verifying of exposure records has been started.

Environmental sciences.—Under contract with Health Research Inc., of New York State, a comprehensive scheme of field collection and laboratory assay procedures pertaining to the total exposure of selected population groups is being conducted. The findings from this study will then be applied to our other field studies.

With the establishment of the Las Vegas and Montgomery laboratories, the scientific personnel at the Sanitary Engineering Center in Cincinnati, Ohio, have been relieved of much of the load of laboratory analysis of environmental samples, and are concentrating their research on radiochemistry, radiophysics, and radiobiology. One study is being carried on to determine to what extent the physical, chemical, and biological factors in a stream act on the removal of radionuclides from water. Laboratory procedures are currently being established.

Also, at the Sanitary Engineering Center a pilot study has been completed on infant dietary radionuclide intake and excretion to provide a methodology for use in further, more extensive studies.

Radiological biology.—Research work has been started at the Southeastern Radiological Health Laboratory in Montgomery, Ala., in the fields of tissue culture, molecular biology, and histopathology. A small animal colony has been established. The nucleus of a scientific staff has been recruited and basic equipment installed. The protocols have been established and cooperative agreements are being negotiated for the conduct of a national study in which 25 medical centers in 12 States thus far have indicated participating interest, on the late effects of radioiodine therapy among hyperthyroid patients.

A tri-State study in cooperation with the health departments of Minnesota, Michigan, and Colorado has been started to investigate cogenital malformations possibly resulting from background radiation. Data are being gathered on incidence of malformations at birth and the populations are being followed up and identified.

Exposure reduction and control.—The first phase of developing methods for the removal of strontium 90 in milk by ion exchange has been completed. This study, conducted in cooperation with the Atomic Energy Commission and the Department of Agriculture, has demonstrated the laboratory feasibility of this removal process. In the second phase which is now underway we are proceeding to build a larger-scale pilot plant.

Laboratory and surveillance activities.—The Radiological Health Laboratory at Rockville, Md., was opened this year. The primary functions of this laboratory are to develop methods for the effective control of radiation hazards from medical, dental, and industrial X-ray units. Training will also be provided to radiological health specialists so they may perform comprehensive surveys of X-ray units.

Since last March, the Public Health Service has increased from 10 to 60 the number of milk network sampling stations, with the result that there is now at least one station in virtually every State making periodic collections of milk to be analyzed for radioactivity at the Service laboratories at Las Vegas and Montgomery.

The Southeastern Radiological Health Laboratory has developed a capability for handling food samples up to 30 pounds, and large marine specimens by ashing. This capability has enabled the radiological intelligence network and environment survey project to move forward in their sampling efforts.

The Southwestern Radiological Health Laboratory has developed a capability for determining radium 226 by the radon emanations methods and in addition has developed procedures and techniques for the quantitative determination of various ions by the flame photometric procedure. This will enable the Southwestern Radiological Health Laboratory to process samples more rapidly.

2. *Technical assistance to States*

Full-time technical staffs have been assigned to six regions with part-time trained consultants in the remaining two regions.

Eleven technically trained officers have been assigned to State departments of health.

An on-site program inventory and evaluation of State resources and activities is now completed for 47 States.

The staff of the Division of Radiological Health has worked closely with the Council of State Governments and the Atomic Energy Commission in its development of first, a model law entitled "State Radiation Control Act," approved and distributed by the Council of State Governments in 1960, and second, the attendant rules and regulations which are now in the process of coordination and final action.

To aid the States in reducing unnecessary exposure among patients receiving medical and dental X-rays, and to personnel operating X-ray units, the Division is increasing its activity in conducting local and statewide surveys of X-ray units.

On-the-spot surveys of dental X-ray machines have been conducted in Montgomery and Prince Georges Counties, Md. (pilot studies) and the State of New Mexico in which all of the State's dental X-ray units were surveyed (268 in all).

A recent development by the Division is expected to expedite greatly the completion of additional dental X-ray surveys. This is the "Surpak method," a unique means of evaluating dental X-ray machines. It consists of mailing out a sensitive sheet of film to each dentist or organization in the survey area, exposure of the film by the dentist to the rays from his X-ray machine, and return of the film, by mail, to the Division of Radiological Health Laboratory in Rockville. Here, through interpretation of the exposed portion of the film, several important safety characteristics of the corresponding machine can be determined. Survey results can then be mailed directly back to the dentist, or delivered to him by local health authorities, along with any necessary filtering elements to increase the safety of his machine.

Eleven thousand surpaks will have been mailed out by June 1961. So far, surpaks have been mailed to Indiana, Missouri, North Dakota, and Utah (2,764 in all).

The executive order directing the Department of Health, Education, and Welfare to be the focal point within the Government for collation, analysis, and interpretation of data has been implemented by the regular monthly issuance to scientists and other interested persons of the radiation data being assembled from a great variety of sources.

3. Training

Technical short courses have been increased to 45 weeks of such offerings in fiscal year 1961, with a total of over 1,200 participants.

In 1961, field courses are being given in Florida, North Dakota, Arkansas, Idaho, and Illinois. Courses include the techniques of emergency monitoring and X-ray survey techniques and procedures.

The Division of Radiological Health in 1961 presented for the first time a special 10-week course on engineering aspects of radiological health. Nineteen chemists, scientists, engineers, and university faculty members attended the course.

In another new approach the Division of Radiological Health assisted and supported the St. Louis University School of Medicine in conducting a postgraduate course covering "The Medical Aspects of Radiological Health" for public health officials. The course was attended by 14 physicians, dentists, and veterinarians who have or will have administrative and technical responsibilities in State and Federal radiological health programs.

A total of 85 Public Health Service personnel received Division of Radiological Health sponsorship for outside-the-Service, academic, radiological health-related training. About one-half of this number were assigned to graduate training on a full-time basis.

In 1961 Congress appropriated $500,000 for training grants in the field of radiological health. The Division of Radiological Health established procedures for awarding training grants to universities and other institutions to utilize the $500,000. The subcommittee of the National Advisory Committee on Radiation met in November 1960, reviewed applications from 19 institutions and recommended approval of 9, involving a total of about $350,000. Final action on these first grants has been taken. The remaining 10 applications and additional applications to be received, will be considered at the March committee meeting.

V. WATER SUPPLY AND POLLUTION CONTROL

1. Comprehensive water pollution control activity recent highlights

Initiation of the most complex and most precedent-breaking comprehensive project undertaken to date, the Great Lakes-Illinois River Basin project, which will cost approximately $12 million and take approximately 6 years to complete.

Initiation of comprehensive pollution control projects on the Chesapeake Bay and the Columbia River Basin.

Continuance of the Arkansas-Red River study, where we expect to recommend measures to protect enough water to meet demands for as much as 22 billion gallons daily.

2. Enforcement and interstate cooperation program

Progress since passage of Public Law 660 (to December 31, 1960):

(*a*) Enforcement actions:

Four public hearings conducted.

Twelve formal conferences conducted.

Four conferences required two sessions each.

Two court actions to defend against proceedings instituted by parties to block hearings.

One court action filed as part of the enforcement procedure.

Four thousand five hundred miles of streams involved in enforcement actions.

Twenty-two States included in areas involved in enforcement actions.

Estimated cost of treatment facilities called for as a result of enforcement actions is over $500 million. This estimate includes only about 2,500 miles of the 4,500 miles of streams involved in enforcement actions.

Enforcement action completed in one area of 196 stream miles.

Post enforcement action surveillance being conducted in 12 areas.

(*b*) Data compiled on quality of interstate waters: One hundred and fifty interstate areas.

(*c*) Digests of State water pollution control laws prepared:

Fifty States.
District of Columbia.
Virgin Islands.

Progress in past calendar year:

(*a*) Enforcement actions:

One public hearing conducted.
Two formal conferences held.
One second session conference held.
One court action filed as part of the enforcement procedures.

Two thousand five hundred miles of streams involving enforcement actions.

Estimated cost of treatment facilities called for as result of enforcement actions is over $118 million.

(*b*) Data compiled on quality of interstate waters: One hundred and fifty interstate water areas (includes updating previously assembled data).

(*c*) Highlights of enforcement activities:

Missouri River (St. Joseph area): Suit filed Septembr 29, 1960, in the U.S. District Court for the Western District of Missouri, St. Joseph division. This is the first suit filed as a part of the enforcement procedure authorized by Public Law 660.

Missouri River (Kansas City area): The municipalities in the Kansas City metropolitan area voted to provide a total of $97.5 million for use in abating pollution of the Missouri River.

Enforcement action, except for postaction surveillance, is considered complete in a 196-mile stretch of the Big Blue River, since the treatment which was recommended as a result of the conference held in 1957 is now in operation by all municipalities involved.

3. *Research program*

Highlights in the research program of the past year have been significant developments in the tools of water pollution control administration:

A comprehensive, long-range plan of attack on the problem of waste water reuse was prepared, and a new program, advanced waste treatment research, was initiated. Under this activity, both intramural and extramural research will be conducted aimed at the development of economical processes for the renovation of used waters.

Fecal streptococci have been established as important indicators of sewage pollution. Using specialized identification procedures in addition to routine enumeration, the relative amounts of pollution from human and animal sources have been estimated. These indicators have been especially helpful in assigning sources of pollution in enforcement cases on interstate streams.

Using a bench model activated sludge unit having a 6- to 7-hour retention time, approximately 90 percent of type I poliovirus and about 98 percent of Coxsackie A9 virus were removed. These data indicate that the activated sludge process is an effective method for removing at least two, and probably other enteric viruses, from sewage.

A reflectophotometer was developed to rapidly determine the efficiency of monolayer films used to reduce evaporation from water surfaces. This instrument compares the rate of change from blue to red of an anhydrous cobalt chloride paper disk above an unfilmed surface with that of a disk above a filmed surface. On water with an established bacterial population consisting of Pseudomonas and/or Flavobacterium, hexadecanol, or octadecanol films rapidly lose their suppression efficiency unless the films are continuously replaced.

The amount of copper tolerated in sewage and industrial waste mixtures without reducing the efficiency of biological treatment processes was determined.

Copper fed as copper sulfate and copper cyanide even in concentrations as high as 25 mg. of copper per liter lowered the efficiency of standard activated sludge treatment an average of only 9 percent as measured by the BOD and COD determinations. A concentration of 1.25 mg./1 of Cr on the sewage produces a measurable difference in effluent quality. Concentrations in the sewage feed above 10 mg./1 interfere with sludge digestion.

A laboratory investigation revealed that appreciable quantities of gasoline, oil, and lead in outboard motor fuels are transferred to the water via the exhaust. The quality of the water in which a motor was operated was damaged for domestic purposes through addition of lead and odorous materials removed only by considerable activated carbon. The water also was toxic to fish and gave them an unpalatable flavor. Severe pollution would result apparently only under conditions of unusually low water volume per unit of fuel consumed. In some situations, however, outboard motor exhaust could make a significant contribution.

Large scale collection and recovery appartus for studying organic chemicals in water was applied to a highly polluted stream. Where only grams of contaminants were recovered heretofore, pounds are now recovered, thus permitting physiological testing, finding individual contaminants including synthetic organics never previously isolated from water, and development of gas chromatographic separation techniques to measure and identify organic contaminants.

It has been demonstrated that algae can readily utilize the phosphate carriers in household detergents as the sole phosphate source for growth. In screening 275 actinomycetes for production of natural algicides, 40 percent showed some degree of antialgal activity. In all instances the more promising antialgal substances produced were completely excreted into the environment and could not be separated from the water by any of the common organic solvents.

Experiments on the dissolved oxygen requirements of hatching coho salmon eggs and developing fry have indicated that these requirements are temperature dependent and that water velocity also is an important factor. The swimming performance of juvenile coho salmon improved progressively as oxygen concentration increased toward air saturation.

4. Basic data program

Progress has been made as follows:

Water quality data now are being obtained regularly from 76 key sampling points on important interstate waters—up 16 from the 60 sampling points established in the first 2 years of the program. Data collection in the past year has required about 80,000 water quality determinations on 6,200 samples of water.

Regular reports on water and sewer bond sales, added to reports on construction, have continued to supply valuable economic data on water quality management.

Collection, publication, and analysis of inventories of water and waste treatment facilities have been made truly national in scope, and are operating on a reliable schedule.

Data on fish kills caused by polluted water are being assembled routinely and have given added impetus to the cause of water pollution control.

Steps are well underway to prepare an inventory of waste water disposal practices at Federal installations throughout the United States.

5. *Technical assistance*

Recent highlights have included: The principles of the waste stabilization pond are being applied to aid small industry in dealing with waste disposal problems. In the past, these principles have been successfully applied in certain instances to the waste disposal problems of suburban communities.

The field study of pesticides conducted in cooperation with State and other Federal agencies is progressing, with sampling and analysis of the surface waters being conducted in several areas of the Southeast to determine the public health and water quality significance of these pesticides.

A study has been undertaken in cooperation with States and other interested agencies to preserve the water quality of Lake Tahoe-Truckee River watershed.

6. *Grants for water pollution control programs*

Recent highlights have included: Under the stimulus of Federal grants, extension and improvements have taken place in all aspects of State programs, notably in establishment of water quality monitoring networks; stepped-up enforcement activities; intensified public information and promotional efforts; and initiation of research projects. In addition to Federal funds, a 54-percent increase in State-appropriated expenditures and a 63-percent increase in personnel since 1956 have made these achievements possible.

7. *Research grants*

In 1961, the number of research grants awarded increased to 161 from 130 in 1960.

Past experience suggests that 333 applications for new and continuation grants will be received in 1962 and that 60 percent of these (208) will be approved for funding.

8. *Waste treatment works construction grants program*

The 2,531 projects approved to date will improve the quality of water in over 28,000 miles of stream for use as public and industrial water supplies, propagation of fish and wildlife, recreation, agricultural, and other legitimate uses.

	Number	Estimated project costs (in millions)	Grants made or requested (in millions)
Grant offers made (July 30, 1956–Dec. 31, 1960)	2, 531	$1, 217. 2	$208. 0
Projects under construction	690		
Projects completed	1, 311		
Projects awaiting construction	530		
Additional applications being processed in regional offices and State agencies	502	294. 1	53. 5
Total applications approved and in process	3, 033	1, 511. 3	261. 5
Activities during calendar year 1960:			
Grant offers made	575	278. 7	44. 8
Projects placed under construction during year	580		
Projects completed during year	483		

TUESDAY, MARCH 21, 1961.

MEDICAL CARE AND FOREIGN QUARANTINE

WITNESSES

DR. JAMES V. LOWRY, CHIEF, BUREAU OF MEDICAL SERVICES
DR. ANDREW P. SACKETT, CHIEF, DIVISION OF FOREIGN QUARANTINE
DR. MYRON D. MILLER, CHIEF, DIVISION OF HOSPITALS
DR. KENNETH R. NELSON, CHIEF MEDICAL OFFICER, U.S. COAST GUARD
RALPH RIGGS, CHIEF, FINANCIAL MANAGEMENT SECTION, DIVISION OF FOREIGN QUARANTINE
RALPH BAHN, FINANCIAL MANAGEMENT OFFICER, BUREAU OF MEDICAL SERVICES
HARRY L. DORAN, CHIEF FINANCE OFFICER, PUBLIC HEALTH SERVICE
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	57, 649	64, 372	66, 762
Positions other than permanent	981	1, 139	1, 129
Other personnel compensation	3, 056	3, 025	2, 918
Total personnel compensation	61, 686	68, 536	70, 809
12 Personnel benefits	5, 936	6, 816	7, 013
21 Travel and transportation of persons	2, 067	2, 139	2, 188
22 Transportation of things	1, 271	1, 239	1, 266
23 Rent, communications, and utilities	2, 405	2, 361	2, 337
24 Printing and reproduction	178	185	185
25 Other services	13, 696	13, 964	14, 596
Services of other agencies	2, 038	2, 313	2, 233
26 Supplies and materials	9, 828	10, 130	10, 589
31 Equipment	1, 805	2, 212	2, 343
41 Grants, subsidies, and contributions	1, 009	1, 209	1, 209
42 Insurance claims and indemnities	15		
Subtotal	101, 934	111, 104	114, 768
Deduct quarters and subsistence charges	1, 395	1, 506	1, 705
Total obligations	100, 539	109, 598	113, 063

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	12, 513	12, 832	12, 989
Full-time equivalent of other positions	224	252	252
Average number of all employees	11, 548	12, 183	12, 551
Number of employees at end of year	12, 106	12, 789	12, 966
Average GS grade	5. 1	5. 2	5. 2
Average GS salary	$4, 757	$5, 152	$5, 158
Average ungraded salary	$4, 524	$4, 812	$4, 745

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Indian health activities	45,446	49,723	52,421
2. Foreign quarantine activities	4,405	4,921	5,122
3. Hospital and medical care activities:			
(*a*) Inpatient and outpatient care	45,610	49,541	50,077
(*b*) Dependents' medical care	2,267	2,445	2,422
(*c*) Coast Guard medical services	1,336	1,329	1,326
(*d*) Operation of health units	723	878	935
4. Payments to Hawaii	1,000	1,200	1,200
5. Administration	225	290	289
Total program costs	101,012	110,327	113,792
6. Unfunded adjustment to total program costs: Property or services transferred in (−) without charge, net	−800	−729	−729
Total program costs, funded	100,212	109,598	113,063
7. Relation of costs to obligations: Obligations incurred for costs of other years, net	327		
Total obligations	100,539	109,598	113,063
Financing:			
Comparative transfer, net	−43,677	−47,165	
Advances and reimbursements from—			
Other accounts	−4,846	−5,204	−5,292
Non-Federal sources (42 U.S.C. 221)	−609	−877	−859
Unobligated balance lapsing	194		
New obligational authority	51,600	56,352	106,912
New obligational authority:			
Appropriation	51,600	55,213	106,912
Proposed supplemental due to pay increases		610	
Applied to contract authorization			−529
Contract authorization (new) (permanent)		529	529

Mr. FOGARTY. Dr. Lowry, are you going to lead off?

Dr. LOWRY. Yes, sir, with your permission.

GENERAL STATEMENT

This is a statement on the budget for "Medical care and foreign quarantine, Public Health Service."

The Bureau of Medical Services of the Public Health Service operates programs of medical care and activities that protect the United States against the introduction of diseases from abroad. The medical services for the Federal Bureau of Prisons in the Department of Justice and the farm placement program in the Department of Labor are supported by funds available to the respective departments. Medical personnel assigned to the Maritime Administration, the Coast and Geodetic Survey and the Bureau of Employees' Compensation are funded by these organizations.

The proposed consolidated appropriation title "Medical care and foreign quarantine," in the President's budget provides operating funds for the programs of the Division of Indian Health, Division of Hospitals, the Division of Foreign Quarantine, and the medical service in the U.S. Coast Guard.

At the request of the House Appropriations Committee, a separate 1962 estimate has been prepared for Indian Health Activities. This estimate and the estimate for Construction of Indian Health Facilities have been submitted for consideration of the Appropriations Subcommittee on the Department of Interior and Related Agencies.

The other beneficiaries designed to receive medical services supported by the "Medical care and foreign quarantine" estimate include American seamen, officers and enlisted men of the U.S. Coast Guard, Federal employees who become sick or are injured in line of duty, narcotic drug addicts, and patients with leprosy. Protection of the United States against the introduction of communicable and other diseases from abroad is accomplished through activities at ports of entry and examinations performed in foreign countries.

The quality of medical care provided in the hospitals and clinics of the Division of Hospitals for American seamen, injured Federal employees, and others has been improved in recent years by the provision of more staff and equipment.

Clinical research activities have been initiated and approved medical specialty training is now well developed. Cooperative activities in both training and research are in operation with schools of medicine, dentistry, nursing, and other health professions. These improve the quality of patient care and contribute to medical knowledge and practitioners' training.

The medical and dental services provided at U.S. shore stations and on ships in all parts of the world protect the health of the personnel of the U.S. Coast Guard.

Another year has passed without any of the international quarantinable diseases—such as smallpox, yellow fever, and cholera being introduced from abroad. Although the United States has been free of these diseases in recent years, they occur continuously in many parts of the world and have been brought to disease-free countries by travelers. Continuous vigilance is required with regard to those diseases. Thousands of persons are examined each year by our personnel stationed in foreign countries to make certain that the visa applicants are free of disease that would make them health hazards or unable to be self-supporting.

A statement on the specifics and details on each of the program activities will be provided by Dr. Sackett, Chief, Division of Foreign Quarantine, and Dr. Miller, Chief, Division of Hospitals. Dr. Nelson, Chief Medical Officer, U.S. Coast Guard, is also available to discuss the Coast Guard medical program.

I would like to say that I used a phrase previously that bothers me a little bit, when I say "clinical research activities have been initiated." I think the word "again" should be inserted, because actually research in our hospitals began back in 1880 when Dr. Keenan returned from a tour of duty in Europe and started a laboratory in the hospital at Staten Island. This laboratory eventually grew into what was called the hygienic laboratory, and then it grew into what is now the National Institutes of Health.

So it would be more proper to say we reinitiated clinical research after a period in which our activities were so restricted that it was impossible to do research and to take care of our responsibilities for patient care.

I would, with your permission, Mr. Chairman, ask for a moment for Dr. Terry to speak to the matter of the Indian health appropriation being assigned to the other subcommittee.

Mr. Fogarty. Go ahead, Dr. Terry.

TRANSFER OF INDIAN HEALTH TO INTERIOR SUBCOMMITTEE

Dr. Terry. I would just like to speak for a moment and say we have already had our hearing before the other subcommittee. We received a very cordial reception. And at the same time, I wanted the opportunity to express to this committee our acknowledgment of the tremendous help and support that we have gotten from this committee over the years.

I think that the work of this committee has been what has allowed us to begin to really make some progress. And we have every belief that the other subcommittee will continue to support us, but I want to say thanks to this one.

Mr. Fogarty. Well, Mr. Denton is a member of both committees. I have always said that so long as that responsibility was in the Public Health Service we should do everything we could to render the best of care to these people. They should not be treated as second-class citizens because they are living on reservations.

Who is going to give the statement on foreign quarantine activities?

Dr. Lowry. Dr. Sackett.

General Statement on Foreign Quarantine Activities

Dr. Sackett. Mr. Chariman, I have a statement to submit for the record, and I would also like to summarize it orally.

(Dr. Sackett's statement follows:)

Purposes of the Program

Mr. Chairman and members of the committee, the Division of Foreign Quarantine performs one of the major responsibilities of the Public Health Service, protection of the United States against the importation of diseases. This is accomplished by (1) inspections and the application of measures at ports of entry to prevent the introduction into this country of serious communicable diseases and their vectors from abroad and (2) the medical examination of applicants for visas at designated consulates abroad and medical inspections at ports of entry in this country to prevent the entrance of any alien with a disease or medical condition which is excludable by law or which might add to the problem of disease control and/or the burden of institutional or economic support if the alien were admitted.

WORLD PREVALENCE OF QUARANTINABLE DISEASE

The United States continued to be free of all of the quarantinable diseases with the exception of four cases of human plague of sylvatic (rodent) origin which occurred in remote areas of the country not significant to international traffic. An additional case was laboratory acquired.

Smallpox, cholera, yellow fever are continuously present in many areas of the world and remain a threat to this country because of the possibility of their introduction through international traffic. The increased speed of transport and the increased number of persons traveling into all parts of the world increase the possibility of their spread.

Smallpox.—The preliminary number of smallpox cases reported worldwide during fiscal 1960 was 99,441. Smallpox was present in over 60 international ports and airports and was epidemic most of the year in at least 12. Sporadic cases were reported on board ship in the Near and Far East. On December 23, 1959, an outbreak of smallpox occurred in Moscow, as the result of an imported case from India; 46 cases were reported by January 25; and the area was not declared free of infection until the end of March. An extensive vaccination program was initiated, and quarantine restrictions were applied to all traffic in and out of the city.

Cholera.—Cholera, which had been confined mainly to India and East Pakistan, spread to West Pakistan and to Afghanistan where it had not been reported since 1946. Contiguous countries in the vicinity of the Persian Gulf placed strict quarantine restrictions on all incoming traffic.

Yellow fever.—Yellow fever is continuously present in the jungle areas of Central and South America and Africa. Sporadic cases were reported in Brazil and Colombia and an outbreak of yellow fever occurred in the Blue Nile Province of the Sudan, with over 100 cases and 87 deaths reported. It has made its appearance in Trinidad twice during recent years. This disease is significant to any country in which the *Aedes aegypti* mosquito exists. This mosquito is prevalent in Hawaii, some of the Southern States, Puerto Rico, and the Virgin Islands.

Plague.—Plague was not reported in any international port. Twelve countries of Asia and Africa, and the port of Singapore caught nearly 2 million rats and examined over 270,000, but none were found positive for plague. Such vigilance is necessary as the disease continues to exist in the wild rodent population of many countries and, under certain conditions, can spread to urban areas and thus into international traffic.

Typhus (louseborne).—Sporadic cases of typhus were reported during the year in Mexico, including the Federal district; and a few cases were reported by countries of South America and Africa. The disease was both endemic and epidemic in Ethiopia and was at a low endemic level in Yugoslavia.

Relapsing fever (louseborne).—Only single cases of relapsing fever were reported by a few countries with the exception of Ethiopia where the disease was both endemic and epidemic.

There are several factors that have contributed to intensifying the risk of introducing quarantinable and other serious communicable diseases into this country from areas of the world where these diseases are still prevalent. Of major importance are the increasing speed, range, and volume of international air traffic. In this jet age, time and distance have been telescoped but the incubation periods of diseases have remained the same. It still takes about 14 days, for instance, for smallpox to develop after exposure to the disease. A traveler can reach this country from any area in the world in less than 3 days, long before the symptoms of the disease would be evidenced. Insect vectors of such diseases as encephalitis, yellow fever, malaria, or sleeping sickness find easy passage by plane or vessel unless specific measures are taken to prevent this. Inland cities are now beginning to receive international traffic whereas it formerly was confined to ports of entry at the borders. Additional airports are being built or existing facilities enlarged to accommodate the giant jets and their passengers. The number of peak arrival periods has increased. New countries are being established with unprecedented rapidity, some of them under internal chaotic conditions, and it is difficult to assess at this time the adequacy of health structures and accuracy of reporting. Thus are sharpened the problems of adequate inspectional coverage for the application of preventive measures against the introduction of disease.

THE QUARANTINE FUNCTION

The quarantine function (inspection and application of preventive measures at U.S. ports of entry) is performed at over 300 points in the United States and its possessions.

The volume of work performed by the Division of Foreign Quarantine will continue to increase in relation to improvements in transportation facilities. In fiscal year 1960, about 5.2 million persons—both aliens and returning citizens—subject to quarantine inspection arrived in the United States. It is estimated that this figure will reach 5.6 million persons in fiscal year 1962. This increase will be largely accounted for by arriving air passengers. No major change is foreseen in passenger traffic by vessel or in the number of persons entering the United States by land from contiguous countries.

The effect of travel by jet aircraft is evident in the increased workload at major international airports. As the airlines continue to convert to jet aircraft with larger passenger capacity, greater speed, and higher frequency of arrival, the quarantine workload will continue to increase.

A survey of flights from nonexempt areas was recently conducted at the Los Angeles Airport. The results illustrate the problem with which we deal. Two flights originating in Denmark were selected on a sampling basis. One hundred and sixty-two passengers had made visits within the 14 days prior to arrival to 21 different European countries, 6 countries in the Near East, 2 countries in Africa, and 1 in the Far East. It can be seen from these examples that even flights originating from Northern Europe have real and direct potential for introducing diseases if our quarantine requirements are not strictly enforced.

In 1960, smallpox vaccinations were given to approximately 526,000 persons subject to quarantine inspection, who did not present valid vaccination certificates on arrival in the United States. It was necessary to detain for medical observation 37 persons arriving at U.S. ports of entry, because of possible recent exposure to a quarantinable disease. Some 54,000 incoming travelers were allowed to continue to their destinations in the United States, but were required to be under medical surveillance for a time. In 1960 the total number of travelers detained or permitted to continue traveling under medical observation comprised 1.1 percent of all persons who were subject to quarantine inspections. The great majority of travelers to the United States comply with our immunization requirements. This is a clear indication of the effectiveness of having and enforcing health requirements.

Progress has been made in eliminating or greatly reducing the yellow fever mosquito, *Aedes aegypti,* in nearly 150 international traffic areas. However, this important mosquito occurs in areas adjacent to airports and docks outside quarantine jurisdiction, thus providing a continual threat of reinfestation. It is necessary to continue the mosquito control program and maintain close vigilance in the international traffic areas as long as the surrounding environment is mosquito infested.

Funds have been carried in this appropriation for investigations on the development of techniques for eradication of the *Aedes aegypti* mosquito, the most common vector of yellow fever. In 1962 these funds are included in the appropriation, "Community health activities, Public Health Service." The Division of Foreign Quarantine will continue its surveillance and control activities in connection with the *Aedes aegypti* mosquito in and around airports and seaports.

In addition to the responsibilities for control of the quarantinable diseases required by international agreement, the Division program includes prevention of the introduction into the United States of other communicable diseases. Additional emphasis in the inspection program of vessels arriving from foreign ports has resulted in improvements especially in food sanitation.

Funds were provided in the 1961 appropriation for 32 positions (of which 20 were added by the Congress) to meet the mounting requirements for inspectional services resulting from the current and expected increase in international traffic and the higher passenger volume of jet aircraft. The general imposition of the 3 percent employment reduction in 1961 permitted filling of only 17 of these positions. Funds are included in this 1962 estimate for activation of the remaining 15 positions and for 8 additional positions at international airports.

THE ALIEN EXAMINATION PROGRAM

Public Health Service examinations at consulates abroad.—Aliens are medically examined by Public Health Service personnel at 22 of the principal U.S. consulates in Europe, Canada, Mexico, and Hong Kong, as part of the requirement for securing a visa to enter the United States. During fiscal year 1960, more than 173,000 alien visa applicants were examined by Division of Foreign Quarantine medical officers assisted by local physicians under their direct supervision. In the performance of these examinations, notifications of significant physical or mental conditions were issued to consular authorities in more than 44,000 cases. Included in this number examined were some 1,600 aliens found to have diseases or conditions excludable under the immigration law, some 15,000 additional aliens found to have disease or conditions which might affect their ability to earn a living in this country, and more than 27,000 cases of disease or physical defects of minor significance.

Non-Public Health Service examinations at consulates abroad.—At consulates where we have no staff, an estimated 135,000 visa applicants were medically examined by foreign physicians selected by the Department of State.

On request of the Department of State, Public Health Service physicians can provide minimal supervision of these foreign physicians in some localities.

Public Health Service medical inspections at ports of entry.—Aliens arriving at U.S. ports of entry are inspected in accordance with the requirements of the Immigration and Nationality Act. This includes those mentioned above who were previously examined abroad for visa issuance purposes as well as visitors, foreign seamen, students, etc. In addition to those already examined abroad in the visa issuance process this group includes alien visitors, seamen, parolees, students, etc. The number of inspections of arriving aliens increased from about 2,700,000 in 1959 to more than 2,900,000 last year. It is estimated that the number of inspections of aliens will reach 3,380,000 in 1962, an increase of 16.5 percent over 1960.

Among the aliens inspected in 1960 more than 41,000 had diseases or conditions reportable to the Immigration and Naturalization Service. This number includes 22,000 with conditions possibly affecting their ability to be economically self-sustaining in the United States, and more than 17,000 aliens with diseases or conditions of lesser significance, and some 2,300 having excludable diseases or defects. Among the aliens identified as excludable upon arrival at U.S. ports, about 600 had been so diagnosed abroad, and were admitted under special provisions of the immigration law. The remaining 1,700 were identified for the first time through examination at the port of entry. (The majority of these were Mexican border crossers and foreign seamen who through our routine examination of aliens were found to have an excludable disease.)

REQUIREMENTS FOR 1962

An amount $5,122,000 is requested to carry out the responsibility of the Division of Foreign Quarantine to protect this country against the introduction of diseases from abroad. The increase of $201,300 over the 1961 appropriation will be used primarily to meet (1) mandatory increased personal service costs and (2) the cost of eight additional quarantine inspectors at seven international airports.

Dr. SACKETT. Mr. Chairman, and members of the committee, the Division of Foreign Quarantine carries out one of the major responsibilities of the Public Health Service—the protection of the United States against the importation of disease. This is accomplished by medical inspections at ports of entry of persons and things entering the country and by the medical examination abroad of applicants for visas.

QUARANTINABLE DISEASES

During the past year no case of quarantinable disease was introduced into this country. The quarantinable diseases are smallpox, cholera, yellow fever, plague, typhus, and relapsing fever.

These diseases still exist in endemic and epidemic form in large areas of the world. During the past year smallpox and cholera were transmitted on numerous occasions from one country to another through international travel, including the introduction of smallpox from India into Moscow, U.S.S.R., where it was contained only after a massive effort.

In recent days, we have learned that there is currently an epidemic of smallpox in Madrid, Spain, the original case of which also came from India.

Speed of international air travel continues to increase. Likewise, it is estimated that the volume of traffic will continue to rise. For example, in the budget year it is estimated that 5.6 million persons, an increase of 400,000 over 1960, including both aliens and returning citizens, will be subject to quarantine inspection on arrival in the United States.

This increase will be largely accounted for by arriving air passengers. A significant portion of this traffic is from areas which are infected with quarantinable diseases. For example, on two flights arriving at Los Angeles from Denmark, visits by the 162 passengers had been made, within the 14 days prior to arrival, to 21 different European countries, 6 countries in the Near East, 2 countries in Africa, and 1 in the Far East. Thus it can be seen from this example that even flights originating from Northern Europe have real and direct potential for introducing diseases if our quarantine requirements are not strictly enforced.

Last year 99 percent of persons entering this country complied with our immunization requirements. This shows the effectiveness of having and enforcing health requirements. The majority of the remaining 1 percent were placed under surveillance and a few were necessarily isolated.

YELLOW FEVER

Progress has been made in eliminating or greatly reducing the prevalence of the yellow fever mosquito, *Aedes aegypti*, in nearly 150 international traffic areas. It is necessary to continue the mosquito control program and maintain close vigilance in the international traffic areas as long as the surrounding environment is mosquito infested.

Our program for maintenance of sanitary standards for ships and airplanes to prevent the introduction of diseases was improved during the past year. Additional emphasis in the inspection program of vessels arriving from foreign ports has resulted in improvements especially in food sanitation.

EXAMINATION OF ALIENS ABROAD

In our visa medical examination program at some 22 consulates abroad, 173,000 aliens were medically examined by Public Health Service physicians and Public Health Service employed and supervised local physicians. Of these, 44,000 were found to have conditions requiring notification to the visa sections of the consulates; 1,600 had diseases such as tuberculosis, leprosy, severe emotional disorders, mental deficiency, and epilepsy, which are excludable under terms of the Immigration and Nationality Act. There were 15,000 found to have conditions which might affect the ability of the applicant to earn a living, and 27,000 were found to have other minor conditions.

At consulates where we have no staff, some 135,000 aliens were medically examined by foreign physicians selected by the Department of State. On request of the Department of State, Public Health Service physicians provide minimal supervision of those foreign physicians in some localities. Alien arrivals, totaling 2,900,000 last year, were inspected at ports of entry into the United States in accordance with the requirements of the Immigration and Nationality Act. This includes those mentioned above who were previously examined abroad for visa issuance purposes as well as visitors, foreign seamen, students, and so forth.

An amount of $5,122,000 is requested to carry out the responsibility of the Division of Foreign Quarantine to protect this country against the importation of diseases from abroad. The increase of $201,300 over the 1961 appropriation will be used primarily to meet (1) mandatory increased personal services costs and (2) the cost of eight additional quarantine inspectors at seven international airports.

Mr. Chairman, that completes the summary of my opening statement.

Mr. DENTON. Dr. Miller, do you want to give us your statement?

Dr. MILLER. Yes, sir.

Dr. LOWRY. Dr. Miller is Chief of the Division of Hospitals, Mr. Denton.

DR. MILLER'S BIOGRAPHY

Mr. DENTON. Have you been before the committee before?

Dr. MILLER. No, sir. I have not.

Mr. DENTON. Before you start out, would you give us just a little bit about yourself, your experience, training, and so forth?

Dr. MILLER. Yes, sir. I was born in Van Wert, Ohio. I had most of my subprofessional education in the State of Ohio, including undergraduate work at Ohio State University. I received my medical degree from the University of Louisville, and following my internship in Buffalo, N.Y., I returned to Columbus, Ohio, and entered a hospital where I received training and experience in internal medicine, including diseases of the chest.

In 5 years, I was appointed director of that hospital, which position I held for 12 years. During that same period, I had appointments as associate professor of medicine at Ohio State University, and assistant director of health for Columbus and Franklin County in tuberculosis control.

I entered the Public Health Service in 1945, in the Division of Tuberculosis Control and soon thereafter entered the University of Michigan where I received my masters degree in public health, and returned to the Division of Tuberculosis Control. Later I was, for a short period, with the Division of Hospital and Medical Facilities.

In 1948, I entered the Division of Hospitals, and was appointed as medical officer in charge of the Neponsit Beach Hospital, which later was moved to Manhattan Beach.

Following that, I was appointed Assistant Chief of the Division of Hospitals, and from there I served 4 years as medical officer in charge of the Seattle Public Health Service Hospital. Then I entered the Division of Indian Health, and was responsible for the hospital program of that Division until January 1960, when I returned to the Division of Hospitals, where I am now assigned.

GENERAL STATEMENT ON HOSPITAL AND MEDICAL CARE ACTIVITY

Mr. DENTON. Now go ahead and give us your statement.

Dr. MILLER. Thank you. I have a general statement and a summary.

(Dr. Miller's statement follows:)

PURPOSE OF APPROPRIATION

Mr. Chairman and members of the committee, the "Medical care and foreign quarantine" appropriation includes funds for the program of the Division of Hospitals which provides health services to beneficiaries designated by the Congress. The principal groups are: American seamen, officers and enlisted personnel of the U.S. Coast Guard, officers of the Coast and Geodetic Survey, commissioned personnel of the Public Health Service, dependents of commissioned and enlisted personnel of the Coast Guard and of commissioned personnel of the Public Health Service under the Dependents' Medical Care Act, persons addicted to narcotic drugs, Federal employees injured in the line of duty, and persons afflicted with Hansen's disease. This appropriation also provides for reimbursement to the State of Hawaii for the care of patients with Hansen's disease in the Hawaiian Islands.

In addition to these beneficiary groups, medical services are provided on a reimbursable basis to members of the Armed Forces and their dependents under the medicare program, foreign seamen, certain beneficiaries from other Federal agencies (Immigration and Naturalization Service, Veterans' Administration, Bureau of Prisons, State Department, Maritime Administration, etc.), and to Federal employees under the Federal employee health programs.

FOUR PHASE IMPROVEMENT PROGRAM

In past statements before your committee, you were informed of serious shortcomings of the resources for providing medical care to patients. Recognizing these needs, the Congress has provided funds which have permitted three stages of a four-phase improvement program aimed at raising the quality of care to an acceptable level by overcoming the shortage of personnel, supplies, and equipment. The improvement program was begun during the 1957–58 period pursuant to findings as reported by outstanding independent specialists in hospital administration who conducted surveys at our hospitals and confirmed our needs.

The Congress approved funds in 1960 and 1961 which made possible the second and third phases of the four-part program. The present estimate provides for the fourth phase of improvement in professional and allied staffing and for supplies and equipment.

Increases received to date in manpower, supplies, and equipment have considerably improved the quality and standards of medical care for patients in our hospitals: medical, nursing, and other personnel shortages have been reduced; additional supplies and drugs have been made available for patients; deficiencies in diagnostic and therapeutic equipment have been lessened; palatability and nutritional value of patient food has been improved; rising costs of utilities and other services have been met. The hospitals are approaching a level of medical care that is more nearly commensurate with present concepts of modern medical practice in comparable community hospitals. The estimates before you represent the fourth stage of this improvement program. The Division of Hospitals will continue its appraisal of programs for effectiveness, economy, organization, and functional operations.

The estimate for 1962 reflects closure of the Manhattan Beach tuberculosis hospital for the entire fiscal year since it was closed on June 15, 1960. Only standby maintenance of the physical plant will be necessary throughout fiscal year 1961.

TRENDS IN PATIENT LOADS

Inpatients.—In the past 5 years, admissions to our 12 general hospitals have increased by 7 percent from 42,516 during fiscal year 1956 to 45,523 during fiscal year 1960. The fiscal year 1962 budget anticipates that admissions will further increase during fiscal year 1962 to 46,300. During this same 5-year period, the average daily patient load in our general hospitals declined slightly from 2,748 in fiscal year 1956 to 2,641 in fiscal year 1960. The decline in the average daily patient load resulted from a decrease of 2.5 days in the length of stay from 23.7 days to 21.2 days during this period.

Admissions to our specialty hospitals (excluding Manhattan Beach, which closed in June 1960) during the 5-year period declined slightly by 134 from 4,826 in fiscal year 1956 to 4,692 in fiscal year 1960. The average daily patient load in these hospitals during the period was reduced from 2,323 in fiscal year 1956 to 2,196 in fiscal year 1960 which is 376 patients above the constructed bed capacity of the hospitals.

Outpatients.—Outpatient visits to all our facilities during this 5-year period have increased by 133,000 or 13 percent from 1,042,000 to 1,175,000. We estimate that the number of outpatient visits will increase to 1,184,000 in fiscal year 1962. The increase in the outpatient workload has resulted in overcrowding of many of our inadequate outpatient facilities.

OTHER FUNCTIONS OF HOSPITALS

The hospitals and clinics of the Division of Hospitals serve important purposes in addition to the provision of curative, preventive, and restorative services for legally designated beneficiary groups. They have been for many years the major source of recruitment for the Service's medical, dental, and other officers. Their internship and medical specialty training programs contribute to the training of the Public Health Service and the Nation's medical and dental manpower.

The hospital system has the potential of serving other purposes within the context of the total Public Health Service mission. The hospitals provide a setting for studies on methods to improve the utilization of medical and nursing services.

RESEARCH

As a result of action by the Congress in 1960 in authorizing PHS grants to the hospitals, a program has been initiated to increase research activities which do much to attract and retain highly qualified staff, improve the quality of medical care, and produce research results of value.

An environment charged with scientific curiosity and disciplined skepticism is necessary to the provision of medical care of high quality. In the PHS hospitals this research environment has contributed to their high standards of patient care and to the increased effectiveness of the individual physician. Research makes possible the atmosphere of inquiry and opportunities for clinical investigation so essential in medical specialty training programs. In addition, the abundant and uniquely diversified diseases of the patients offer an invaluable resource for large scale therapeutic evaluations of new drugs. An example is the present PHS "Cooperative Drug Study" for the clinical evaluation of antihypertensive drugs which is geared to the eventual capability of other drug trials in the field of clinical pharmacology. Current research in the PHS hospitals includes 55 individual projects, several of which are in collaboration with university medical schools; six are supported by PHS grants; the remainder are supported directly by the Division of Hospitals. Past accomplishments of the clinical research in the hospitals include the penicillin treatment of syphilis, the sulfone therapy of leprosy, and the treatment of certain forms of cancer by the technique of isolated perfusion. Current research includes the study of diseases of the heart, cardio-pulmonary abnormalities of function under stress of exercise, correlation of anatomical and biochemical changes in kidney disease, clinical drug trials in cancer, and a variety of projects on leprosy. The potential for clinical research in the PHS hospitals is a promising source of contributions to medical knowledge. We are requesting funds to support eight additional positions and necessary equipment for this program in fiscal year 1962.

ADMINISTRATION

We are embarking upon several programs designed to improve administration and management in our hospitals.

Automatic data processing.—We have instituted pilot studies in data processing at our Baltimore and Staten Island hospitals. These initial efforts concern financial management. We plan to extend our explorations into other management areas during the coming year.

Staffing surveys.—With the encouragement and assistance of the Office of Financial Management of the Secretary's Office, a study was started to develop a method for relating hospital staffing requirements to the kind and volume of workload. The hospitals at Baltimore and New Orleans were used as sites for pilot studies. Surveys of other hospitals will be conducted in order to test the method. This is a pioneer program in hospital administration and is arousing interest on the part of other hospital administrators. Mr. Ray Brown, superintendent of the University of Chicago Clinics, who is a recognized authority on hospital administration, is serving as consultant in this program. This study could provide an objective method for evaluating and determining the staffing needs of hospitals.

Management development.—In October a conference on administration for department chiefs was conducted at our Lexington hospital. In its broad task of providing comprehensive care and treatment of patients, a hospital must divide the total job into many professional, technical, managerial, and clerical tasks, and assign these appropriately among its several hundred personnel. While dividing the work, the hospital must put it together again so that an integrated pattern of service for the patient is attained. Because the staff of the hospital is made up of individuals representing diverse professional, technical, and administrative disciplines, one of the problems confronting the administrator is to establish communication among his staff in a language of common understanding so that their total coordinated efforts as a team may be continually brought to bear on every patient being treated.

The conference at Lexington was an experiment designed to bridge some of the barriers to good communication in hospitals. We plan to explore further this means of improving the operation of our hospitals.

International cooperation.—At the present time, we have in training at our Staten Island, Baltimore, and San Francisco hospitals, hospital personnel from the Philippines, British Guiana, Nepal, and Ethiopia.

Physical facilities.—All of our hospitals were built before 1940. They are functionally unsuited in many respects for the conduct of modern medical care and research and require modernization.

FUND REQUIREMENTS FOR 1962

The 1962 estimate reflects our objective which is to provide continued improvements in medical care afforded our beneficiaries until acceptable standards are realized, including the further development of research programs in our hospitals. The estimate provides for additional staffing in the hospitals to the level that was declared necessary at the time that the 4-year program was initiated; for meeting the requirements of drugs for patients for necessary supplies and for the purchase of scientific and other equipment needed in 1962.

A net increase of $567,400 will make available for this activity a total of $54,160,400 in 1962. The increases and decreases reflected in the estimate are as follows:

Mandatory increases:	
Annualization of 1961 pay raise	$35, 000
Additional cost for within grades and incentive pay increases	92, 000
Annualization of 1961 wage board increases approved through September 15, 1960	2, 000
Total mandatory increases	129, 000
Program changes:	
(*a*) Inpatient and outpatient care:	
(1) 27 additional personnel and related costs	154, 000
(2) Elevation of patient supply and drug issues	196, 000
(3) Equipment for outpatient clinics moving to new Federal space	80, 000
(4) Net change in other objects	10, 000
(5) 8 additional personnel and equipment for research	76, 000
Subtotal	516, 000
(*b*) Operation of health units: 10 additional personnel and related objects for new health units	59, 000
(*c*) Coast Guard medical services: Decreases in equipment	—3, 000
(*d*) Dependents' medical care: Decreases in estimated costs	—23, 000
Net program increases, hospital and medical care activities	549, 000
Other decreases:	
1 less day's pay in 1962	—45, 000
Reduction in 1962 wage board increases funded in 1961	—65, 000
Total other decreases	—110, 600
Net increase hospital and medical care activities	567, 400

Mr. DENTON. We will be glad to have you summarize your statement.

Dr. MILLER. Mr. Chairman and members of the committee, I wish to thank you for affording me this opportunity to present you with a brief statement of progress that has been made in operations of the Division of Hospitals; and I should like to point out areas where further improvements, as outlined in the budget before you, are desirable in order that we may provide adequate medical services to our patients. Your sincere interest and support have been largely responsible for the many improvements that have been made in recent years. You have done this, we believe, because you have been aware of our accomplishments, our needs, and our problems.

Appropriation increases granted over the past several years have enabled us to add critically needed personnel, supplies, and equipment; to meet the rising costs of hospital operation; and to correct many of the deficiencies which you have known to exist.

In previous hearings you have been apprised of a planned program to meet personnel shortages by adding professional and supporting staff to our hospitals. This was distributed over a 4-year period. In fiscal years 1960 and 1961 the Congress approved funds which made possible the second and third phases of this program and important accomplishments have been made. The provision of increased personnel, supplies, and equipment has elevated the medical standards in our hospitals to a point where they are approaching a level of medical care more nearly commensurate with modern hospital concepts. The development of research and training programs will provide us with two strong arms which, along with the clinical care of patients, compose a triad necessary for sound medical practice. The 1962 budget requests funds for the fourth phase of strengthening professional and allied staffing, for supplies, and equipment.

CHANGE IN PATTERN OF PATIENT CARE

During the past 5 years there has been a noticeable change in the pattern of patient care. The number of admissions to our general hospitals has increased 7 percent. Improvements in the quality of care and efficiency of operation in the past several years have shortened the average stay of patients by 2½ days. This is beneficial to the patient since he is returned to productivity at an earlier date and it is beneficial to the hospital because the cost of treating the average illness is reduced. It has also resulted in a lower average daily patient census and a higher average daily cost per patient; but despite increased staffing and other improvements, the increased daily cost is less than the consumer price increase for non-Federal hospitals in this country. Further progress will be dependent, in part, on modernization of the hospitals so that the staff can work more efficiently.

Although there has been a slight decline in the number of admissions to our specialty hospitals for patients with narcotic drug addiction and leprosy during the past 5 years, the present census is still 376 patients above the constructed bed capacity of these hospitals.

There has been a continuous increase in the number of outpatient visits to our hospitals and clinics. This upsurge to about 1,200,000 visits per year has occurred more rapidly than expansion of space and improvement of facilities. It has been impossible to preserve an acceptable level of patient care and to utilize personnel efficiently in our outpatient areas.

Hospitals and clinics of the Division of Hospitals serve important purposes in addition to the provision of diagnostic, therapeutic, and preventive medical care of legally designated beneficiary groups. For many years they have been a major inlet for recruitment and a source of trained physicians and other professional and supporting personnel for the entire Service. Recruitment of career officers has been largely through the several internship programs. Professional personnel trained in medical specialties by the Division of Hospitals have significantly contributed to the staffing and operation of other divisions and institutes of the Public Health Service. Within the Bureau of Medical Services the comparatively new Division of Indian Health has been the recipient of many officers so trained, as well as physicians, pharmacists, dentists, and other professional officers without specialty training.

RESEARCH ACTIVITIES

As a result of action by the Congress last year in providing funds for research in our hospitals and authorizing grants from the National Institutes of Health, a very promising research program is developing. These investigational programs not only promise new discoveries but they also attract and retain keen thinking personnel and contribute to the quality of medical care of patients. Current research projects in our hospitals, including those financed by this appropriation, number 55, several of which are in collaboration with outstanding medical schools.

We are embarking upon several programs designed to improve administration and management in our hospitals. These include studies in automatic data processing and analytical staffing studies of personnel requirements in hospitals. Preliminary reports of these latter studies not only appear significant to us but have aroused the interest of outstanding hospital administrators of the country.

We have conducted a management development program in our Lexington Hospital and are presently providing training in hospital administration to four students from foreign nations.

The 1962 estimate which we are presenting to you makes a request for certain increases which are directed toward further improvements in medical care for our beneficiaries through the addition of personnel for the operation of general hospitals, health units, and research programs; for necessary drugs, supplies, equipment, and other items. Certain decreases are also anticipated. The net increase for hospital and medical care activities submitted with this presentation is $567,400.

I shall be happy to answer any questions or explain this presentation in any way possible.

NARCOTIC LAWS

Mr. FOGARTY. Thank you, doctor. Before I forget it, what State in the Union has the best narcotic laws? Does anyone have any idea?

Dr. LOWRY. For the control of narcotic drug traffic?

Mr. FOGARTY. Yes.

Dr. LOWRY. I think if you ask this question of Mr. Anslinger, he would probably tell you Ohio has the best State narcotics laws and the best State enforcement. He could show you what has happened since they passed this law about 5 years ago.

Mr. FOGARTY. Thank you.

Dr. LOWRY. Mr. Fogarty, you have heard the statement from Dr. Sackett and Dr. Miller. Dr. Nelson, the chief medical officer of the Coast Guard, is here. This is the third program area in the Bureau for which funds are contained in this budget.

Mr. FOGARTY. All right. Dr. Nelson, do you want to come forward?

Dr. NELSON. Thank you, Mr. Chairman.

COAST GUARD MEDICAL SERVICES

I do not have a statement, but I appreciate the opportunity to make some explanatory remarks concerning the item in the appropriation.

Mr. FOGARTY. All right.

Dr. NELSON. This item in the appropriation covers the cost of medical and dental care given at Coast Guard installations on land all over the world, and on their vessels and ships at sea.

The land installations are such things as the Coast Guard Academy at New London, Conn., where we have a hospital that takes care of the cadets and military personnel assigned to the Coast Guard Academy. We have training stations at Cape May, N.J.; Alameda, Calif.; Groton, Conn.; and Yorktown, Va.

At these training stations, we have infirmaries and sick bays.

We also have infirmaries and sick bays at air stations at Elizabeth City, N.C.; St. Petersburg, Fla.; Salem, Mass.; and San Diego, Calif.

We have loran stations, concentrations of 25 to 50 men in various isolated places all over the world.

In addition, we have dental trailers that make regular visits to the smaller concentrations of Coast Guard personnel in scattered areas, particularly along the Great Lakes, which are not close to any of the large military installations.

This item also takes care of the emergency medical and dental care which arises in some of these isolated areas which are not close to any large military installation.

Ships on which we have medical officers and fair-sized infirmaries—examples of them are the *Eagle*, which is the training ship for the Coast Guard Academy and on which the fourth year cadets make a trial cruise every year. This cruise lasts for approximately 2 months. We then have a Coast Guard icebreaker which goes to the Antarctic each year. We have the Bering Sea patrol, which goes up into the northern waters and gives care in the isolated areas to Eskimos and other peoples up there who are not close to medical care installations.

We have the ice patrol in the North Atlantic. We have weather ships, four, at all times in the Atlantic, and two in the South Pacific, that carry physicians and large crews.

This whole program takes care of approximately 30,000 enlisted and commissioned regular officers and enlisted personnel of the Coast Guard, and 14,000 reservists that are called to active duty for various periods during the year, and is responsible for their medical care while they are on duty, and their examinations before they enter on duty and before they leave duty.

I appreciate this opportunity of giving a few explanatory remarks concerning the scope of this particular item in the budget.

Mr. FOGARTY. You have about 50,000 men to take care of?

Dr. NELSON. That is correct.

Mr. FOGARTY. You have 105 positions?

Dr. NELSON. Yes, sir; of which 31 are physicians.

Mr. FOGARTY. How does that correspond with the Army and Navy and Air Force?

Dr. NELSON. This is a little difficult at the present time to give you an accurate statement, Mr. Chairman.

Mr. FOGARTY. Well, why don't you supply it for the record, then?

Dr. **Nelson**. I will be glad to.

(The information requested follows:)

Comparison of Physicians Per 1,000 Active Duty Personnel

Army: 3.3 as of June 30, 1960
Air Force: 3.5 as of June 30, 1960
Navy: 4.0 per calendar year 1959
Coast Guard: 0.9[1] fiscal year 1960
Coast Guard: 0.9[1] fiscal year 1961
Coast Guard: 0.8[1] fiscal year 1962

ORIGINAL BUDGET REQUEST FOR COAST GUARD

Mr. **Fogarty**. Did you ask for any funds in addition to what the Bureau of the Budget has allowed you?

Dr. **Nelson**. The request by the Department was for $1,424,000, Mr. Chairman.

Mr. **Fogarty**. What did you get?

Dr. **Nelson**. $1,326,000, sir.

Mr. **Fogarty**. Do you think you need the additional funds?

Dr. **Nelson**. I believe to give the type of medical care that the military forces should have, we should have—we need the amount that the Department——

Mr. **Fogarty**. Will you give us a breakdown of the difference in positions and why you think it is necessary? Supply that for the record.

Dr. **Nelson**. I will be happy to, Mr. Chairman.

(The information requested follows:)

The request to the Budget Bureau for the Coast Guard medical services was in the amount of $1,424,000. This included $933,900 for all expenses for the 105 positions requested, $165,000 for supplies, $15,000 for equipment, and $310,100 for all other expenses. This last part of the estimate was reduced by $95 000 while equipment was reduced by $3,000. The services eliminated by the reduction of $95,000 are as follows.

Dental care for coastguardsmen.—The Budget Bureau review eliminated $50,000 for dental care for coastguardsmen at their duty locations where such care could be furnished at a cost less than the travel expense to the nearest Public Health Service facility.

Medical care at isolated locations.—The review eliminated $15,000 which was requested for nonemergency medical care of coastguardsmen at isolated stations. Such care will be furnished by travel at Coast Guard expense to the nearest Public Health Service facility.

Additional consultant services at the Coast Guard Academy.—The review eliminated $7,500 requested to provide additional specialist fee basis services needed at the Coast Guard Academy at New London, Conn.

More complete physical examinations.—The review eliminated $22,500 to provide for more complete physical examinations of recruits and reservists called to duty. A more complete examination would better screen out the physically unfit and thus reduce the number of early discharges with some Government responsibility for postdischarge care. The request was to provide $7.50 per examination rather than the average of $5 now in effect.

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[1] This item is not comparable to that of the other services. In addition to physicians specifically assigned to the Coast Guard on a full-time basis, medical care is also provided to Coast Guard personnel by physicians in the hospitals and clinics of the Public Health Service, and in offices of designated physicians.

If a proportionate share of physicians in Public Health Service hospitals and clinics is added to the full-time physicians assigned to the Coast Guard, the number of physicians per 1,000 active duty Coast Guard personnel increases to 2.3 in 1960, 2.3 in 1961, and 2.2 in 1962.

Mr. **Fogarty.** All right. Thank you very much, doctor.

Dr. **Terry.** Mr. Chairman, if I may, at this point, I would like to mention that this will be Dr. Nelson's last appearance before this committee. He is set to retire as of May 1, after some almost 32 years in the Service, and is to become the commissioner of hospitals in the city of St. Louis.

Mr. **Fogarty.** Well, it is nice to hear that you are getting such a good position, Doctor.

Dr. **Nelson.** Thank you, Mr. Chairman. Thank you, Dr. Terry.

Mr. **Fogarty.** We are sorry to see you go. We will miss you before the committee. I think you have done a good job in building up the hospitals while you were head of the Division.

Dr. **Nelson.** It was with the help of your committee that I was able to carry the job through. I deeply appreciate it.

Mr. **Fogarty.** The hospitals are in a lot better shape now than they were a few years ago.

SUMMARY OF BUDGET FOR HOSPITAL AND MEDICAL CARE ACTIVITIES

Dr. Miller, your appropriation for 1961 is $48,835,000, and the request is for $49,332,000, an increase of $497,000, and 45 positions.

The only program increase chargeable to appropriated funds is $516,000 for your regular activities at the hospitals and outpatient clinics.

STAFFING OF HOSPITALS

What does the language on page 15 mean—

> * * * the estimate provides for additional staff in the hospitals to the level approaching that previously identified as needed. * * *

Dr. **Miller.** Four years ago we began a program of personnel increases in our general hospitals.

Mr. **Fogarty.** As a result of this special committee that was set up by the Surgeon General?

Dr. **Miller.** This was a result of special surveys that were made to determine the staffing needs of these hospitals.

For 3 years the Congress has granted an increase in the number of personnel. This is the fourth year of the phasing program.

Mr. **Fogarty.** How many years was the program to require?

Dr. **Miller.** Four years, sir.

There was one year, fiscal year 1959, when no increase was allowed in the number of personnel. It actually began in 1958. In 1959 there was no increase, but there were increases allowed in fiscal years 1960 and 1961. This is the fourth year.

Mr. **Fogarty.** How much is the increase this year?

Dr. **Miller.** We are asking for 27 man-years of average employment in our general hospitals, and 8 additional positions in research.

Mr. **Fogarty.** Will that bring it up to the desired level?

Dr. **Miller.** Yes, sir. This will bring us up to the level that was determined to be adequate at the time the 4-year program was started.

Mr. **Fogarty.** Is that program out of date now?

Dr. Miller. That, Mr. Chairman, I am unable to state fully at this time, because we are now making studies to try to determine what our needs will be in professional and supportive staffing in our hospitals.

Dr. Lowry. Mr. Chairman, I think we should state here that this survey had to do with patient care activities only, and is certainly out of date if one is thinking in terms of the training and research activities of the hospitals. But insofar as the patient care activities are concerned, we will be meeting the goal that was set 4 years ago. We are in the process of redetermining this goal to see whether it is realistic in terms of presentday medical needs.

Mr. Fogarty. Well, I was wondering why you used the words "to the level approaching that previously identified as needed." It raised some doubt in my mind as to whether you have all that they said you needed.

How much do you think it would cost to get your medical services up to the proper level?

Dr. Miller. Mr. Chairman, I think we would have to first determine the personnel needs on the basis of the present period in order to know what would be the proper cost.

Mr. Fogarty. Well, can't you determine that, or do you have to have another survey team determine it for you?

Mr. Kelly. Mr. Chairman, I wonder if I might speak to that for a moment. As was pointed out, about 5 years ago the Surgeon General had a group of outside consultants come in and look at each of the general hospitals. They made a general observation, that was pretty unanimous with respect to all of them, that the level of medical care was not up to the level which the Federal Government should be providing. Some of these reports included specific recommendations for staff increases, so many in this department, so many in that. Others just made the general categorization that they were inadequate.

We did not have specific surveys that identified on a point-by-point basis the precise staffing requirements. We did have estimates for each of the hospitals. We arrived at a total staffing requirement which generally equated with equalized veterans' hospitals.

We have since instituted a series of very thorough analytical studies to try to establish the method of determining staff in each hospital for each activity, using workload measurements as the base. The studies have been done on a pilot basis in several hospitals; but they have to be equated, when we finish all of the hospitals, before we can arrive at a final determination as to what this should be for each of the activities.

So I think the testimony was designed to show that we reached the target that we established for ourselves following those other reports, but does not constitute a determination that that target was the appropriate one based on this kind of survey.

COMPARISON WITH VETERANS' HOSPITALS

Mr. Fogarty. Are you satisfied that the veterans' hospitals are a good yardstick to follow?

Mr. Kelly. No, sir; we are not. We have used it for want of something better, and now we are trying to produce that something better that is tailored to these specific hospitals.

Mr. Fogarty. I think the veterans' hospital in my city only has about half the number of personnel per patient as the general hospitals in that area.

Dr. Lowry. This may be true, Mr. Fogarty. However, at that time the veterans' hospitals were so much better staffed than our own, that this was a practical reasonable goal for us to try to achieve.

Mr. Fogarty. Well, I do not know whether it is a good measurement to use, because in many of the veterans' hospitals the type of care is entirely different than the care you provide and the care that is provided in a general hospital. They have many long-term cases, and people in the older age bracket now. So there is quite a difference in the type of patient care given.

Dr. Lowry. That is very true.

Mr. Fogarty. Yours would require more than the average veterans' hospital would require; don't you think?

CONSULTANTS

Dr. Lowry. Yes; they will. As a matter of fact, as Mr. Kelly has pointed out, we are trying to develop a system for evaluating and determining the actual number of individuals required for the particular hospital and the kind of patients they have. In addition to that, we have had two preliminary surveys of our San Francisco and Seattle hospitals by a professional consultant, a surgeon. He has pointed out to us some very important deficiencies in the professional staffing particularly in pathology and radiology and things of that kind.

Mr. Fogarty. Are you satisfied that you are getting good service from this consulting group?

Dr. Lowry. We have a very good consultant group in our committee on hospitals and clinics.

Mr. Fogarty. You think they are worth the money?

Dr. Lowry. They are worth much more than we pay them. We are also about to initiate a study of our hospitals in relation to the medical schools with the National Advisory Health Council, and some deans of medical schools. We hope from this to further improve our working with medical schools, and therefore our services in our hospitals.

Mr. Fogarty. When will you have that study completed?

Dr. Lowry. I would guess that the study will probably require another year to 18 months before each one of the hospitals will be completed. We have used two hospitals essentially as study hospitals to develop the method of doing this. That is Baltimore and New Orleans. As soon as we can get concurrence that this is a proper method, then we will proceed with the rest. I think it would require about 18 months before all the hospitals could be done, if we are successful in getting an acceptable method before the end of this fiscal year.

Mr. Fogarty. Do you think you will have any recommendations this time next year for this committee?

Dr. Lowry. We will have recommendations on those hospitals for which the studies have been completed. We will be pleased to use those.

CLOSING OF THE MANHATTAN BEACH HOSPITAL

Mr. Fogarty. You closed the Manhattan Beach Hospital almost a year ago. Do you feel you are giving just as good service to eligible patients as you were before?

Dr. Miller. The hospital was closed June 15, 1960. Our patients with tuberculosis, who formerly would have been hospitalized at the Manhattan Beach Hospital, are cared for in a very good veterans' hospital and in our general hospitals, including the Staten Island Hospital. I believe they are getting very good care, sir.

Mr. Fogarty. How much money are you saving by closing that hospital?

Dr. Miller. Last year we saved approximately $850,000 by the closure of that hospital.

Dr. Lowry. I don't think you can answer that question by saying you saved that much money. This is the amount of money that was not spent at Manhattan Beach Hospital. But we also had to buy the care for the patients who were hospitalized. The question——

Mr. Fogarty. Well, it may be a difficult question for you to answer right now. Why don't you supply the best answer you can for the record.

(The information requested follows:)

The $850,000 saved in 1961 by the closure of Manhattan Beach Hospital was applied to pay act costs for the "Hospitals and medical care activity."

Dr. Lowry. May I say that we found that our per patient day cost at Manhattan Beach was above the cost that would be necessary to buy the same care from the VA hospital.

RESEARCH PROGRAM AT CARVILLE HOSPITAL

Mr. Fogarty. How is your research program progressing?

Dr. Miller. Our research program is progessing very well, thanks to the assistance that we received from this committee in past years, beginning with the Carville research program in 1959, and the appropriation that was made last year which enabled us to get started on a basic research program in our hospitals. The amount was $100,000.

We are conducting research programs in most of our teaching hospitals, and in our Carville Hospital, and have made very excellent progress to date, sir.

Mr. Fogarty. Are they satisfied at Carville now?

Dr. Miller. I think that they are satisfied that they are moving forward with their research program very well.

Mr. Fogarty. How much did you cut them back from what they asked for this year?

Dr. Miller. For research purposes, sir?

Mr. Fogarty. No; their entire operating budget.

Dr. Miller. I will have to supply that, sir.

Mr. Fogarty. All right. Will you supply that for the record?

Dr. Miller. Yes, sir.

(The information referred to follows:)

The medical officer in charge of the hospital at Carville, La., requested an increase of $100,900 over the $2,196,000 (including provision for civil service pay raise) available for 1961. Of the increase, $43,700 and five positions represented requirements for operating personnel and expenses related to their employment. The amount of $57,200 was requested by the hospital to provide five positions, supplies, equipment, and other needs to augment the research program of the hospital.

The Division of Hospitals approved only $10,000 for two research positions. No increase for the hospital operation proper was allowed.

The $10,000 requested was approved by all reviewing bodies and is included in the 1962 estimate as submitted to the Congress.

Mr. Fogarty. Do you have any other problems at Carville?

Dr. Miller. We are moving along well in the completion of our building program that has been under progress for several years.

Mr. Fogarty. Is that satisfactory?

Dr. Miller. I believe so, sir.

MEDICAL CARE FOR NARCOTIC ADDICTS

Mr. Fogarty. You are still providing services for narcotic addicts?

Dr. Miller. Yes, sir.

Mr. Fogarty. Are you making any headway?

Dr. Miller. With your permission, sir, I would like Dr. Lowry, who formerly was medical officer in charge of the Lexington hospital, to answer that question.

Dr. Lowry. The hospitals have achieved outstanding places in the medical community, particularly in terms of the research on narcotic drug addiction. The hospital at Lexington developed a standard of care for treatment of the physical dependence of narcotic drug addicts that is now used throughout this country and throughout the world.

This is the use of methadone substitution and the treatment of physical dependence.

The hospitals, I think——

Mr. Fogarty. Is Lexington filled?

Dr. Lowry. Lexington is more than filled.

We try not to have it more than 100 percent occupied.

Mr. Fogarty. Do you have a waiting list?

Dr. Lowry. Yes.

Mr. Fogarty. Where is it from—New York?

Dr. Lowry. Most of the waiting list is from New York, some from Chicago, and a few from Detroit.

There is no waiting list for women. There is a rather lengthy waiting list for men, and this——

Mr. Fogarty. What age group?

Dr. Lowry. The addicts that are being admitted now are mostly in their 20's and are mostly colored people from the large cities. These are the ones that are on the waiting list.

This list has accumulated within the last year, and I think that at the present time we will see a further increase in it because the number of people applying for treatment—I am referring to the volunteer patients now—is often related to the availability of the supply of illegal narcotic drugs.

I think within the past year there has been both more effective international control, and if you have been following the problem, you will note that there has been a stepup in the seizures of illegal narcotics coming into this country. Right now there is a real dearth of illegal narcotic drugs, and you will see an increase in the number of people applying for admission to the hospital.

We are getting to the point where we are moving on the only satisfactory prevention of drug addiction, and that is to keep narcotic drugs away from susceptible individuals. As long as we have illegal drugs available to them, we are going to have narcotic drug addicts, and then our hospital will just have to keep doing more and more work trying to treat people who become addicted. This is a very difficult proposition, because narcotic drug addiction is a relapsing disease in individuals who are unstable.

Mr. **Fogarty.** Do you have any addicts in the hospital in Fort Worth, Tex.?

Dr. **Lowry.** Yes.

Mr. **Fogarty.** Do you have many?

Dr. **Lowry.** Their census runs up over 100 percent, and of the total number down there, all except about 350 are narcotic drug addicts. That means about 550 are addicts.

Mr. **Fogarty.** Have you given consideration to services for alcoholics?

Dr. **Lowry.** No, we have not because the basic authorization for the hospitals, if you will recall, is to provide treatment for Federal prisoners and probationers who are narcotic drug addicts. This is the only authorization we have.

Some years ago the addict used to get introduced to addiction through alcoholism, but we do not see that any more.

At that time, we were working with individuals who were both alcoholic and narcotic drug addicts. Today we are not working with the alcoholic.

DEPENDENTS' MEDICAL CARE

Mr. **Fogarty.** Do you really think the cost of the dependents' medical care program will go down $23,000?

Dr. **Miller.** I do not believe there is any way for us to determine. Certainly——

Mr. **Fogarty.** You would not want to bet on it.

Dr. **Miller.** No, sir. I would not want to bet on it.

Mr. **Fogarty.** Are you requesting new language for this program?

Dr. **Miller.** We are asking new language in relation to the deficiency in the dependents' medical care financing for 1959.

Mr. **Fogarty.** What happens if you do not get the language?

Mr. **Kelly.** This we do not know, Mr. Chairman.

Mr. **Fogarty.** Do you have bills on hand?

Mr. **Kelly.** We have bills. This program works through the Defense Department. They have actually paid for the services that were rendered to beneficiaries but the information did not reach us until quite recently. We have been unable to reimburse the Army for the expenses that were incurred. We have reported this to the Congress as having incurred a deficiency on items over which we had no administrative control. It seemed not to be the wisest course to try to submit a supplemental request for it when this bill would be before the Congress; and we have therefore requested it in this regular bill.

OPERATION OF HEALTH UNITS

Mr. **Fogarty**. You have an increase of $57,000 for operation of health units. This is reimbursable. But tell us what occasions the increase.

Dr. **Miller**. We are increasing the services by the addition of health units regularly; this is to include the addition of 6 new health units and the employment of 10 additional personnel.

Mr. **Fogarty**. Now, our Capitol physician, right across the hall is limited in some respects to rendering services to Members of Congress. What, in your opinion, would need to be done to establish a health unit for employees at the Capitol?

Mr. **Miller**. The health units are established upon application from the Federal agency to the Public Health Service for inspection of a plan for developing a health unit.

Mr. **Fogarty**. I don't think the question has been asked before, and I'm not sure about the eligibility of the legislative branch.

Dr. **Lowry**. Mr. Fogarty, I would be pleased to try and answer it for you.

If this particular operating group were to ask us for consultation, we could come and look at what we thought would be an appropriate program that was within the law as it presently is established.

Mr. **Fogarty**. Why don't you supply for the record what you think would be appropriate?

Dr. **Lowry**. We would be very glad to do that.

May I insert one word of caution and that is that we have limitations through an Executive order that will not allow us to do certain things that are presently authorized in the law, but we will be glad to point out that these things should be done in the program that would be recommended.

Mr. **Fogarty**. What changes in law might be necessary if it was to be more effective?

Dr. **Lowry**. Actually, there is no change in the law required. Our Department has made a request of the Bureau of the Budget that the present restrictive Executive order be modified so that we can have programs authorized by the law.

There is another question as to whether the law allows us to establish programs in other than the executive branch of the Government.

Mr. **Fogarty**. What are these restrictions in the Executive order?

Dr. **Lowry**. Well, the law makes provision for periodic examinations. The Executive order limits us so we cannot do what we refer to as periodic examinations. This would be the annual examination for people over 40 years of age, screening for diabetes, for glaucoma, and things of that sort. It also precludes our engaging in preventive medical activities that are authorized in the law. This would include vaccinations and things of that kind.

Mr. **Fogarty**. Place in the record a complete statement covering the points we have been discussing including what is being done to get the Executive order broadened so that it covers the things authorized by the law.

Dr. **Lowry**. We will be glad to do so.

(The statement follows:)

1. Regarding legal authority:

Under the provisions of Public Law 658, 79th Congress, an agency of the Federal Government may, if it has funds available, establish a health program for its employees. Such program shall be established only after consultation with the Public Health Service and consideration of its recommendations. The agency may then either operate its own program or request the PHS to do so on a reimbursable basis.

2. Regarding services which could be provided under a program operated by the Public Health Service:

The law authorizes these services:

1. Preventive programs relating to health.
2. Treatment of on-the-job illness and dental conditions requiring emergency attention.
3. Preemployment and other examinations.
4. Referral of employees to private physicians.

A 1950 Executive order, still in effect, limits the services to the treatment of on-the-job illness, preemployment and fitness for duty examinations, and referral of employees to private physicians. The Executive order does not permit certain preventive programs such as cancer, heart disease, diabetes, or glaucoma detection. An agency health program would be subject to this same limitation, whether operated by the agency itself or by the Public Health Service.

3. Regarding what is being done to modify the Executive order:

In February 1960 there was forwarded to the Bureau of the Budget, by the Secretary, Department of Health, Education, and Welfare, a proposed modification of the Executive order of 1950. To date no action has been taken. In February 1961 the Under Secretary of the Department of Health, Education, and Welfare forwarded to the Bureau of the Budget a memorandum requesting that the proposal submitted a year previously be given favorable consideration.

Mr. FOGARTY. Is there anything further you want to say, Doctor?

Dr. MILLER. No thank you, sir.

Mr. FOGARTY. Thank you very much.

FOREIGN QUARANTINE SERVICE

Dr. Sackett, you had available in 1961 $4,948,800. Your request for 1962 is $5,150,000, an increase of $201,200 and 8 positions.

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. Where are those 8 positions going to be?

Dr. SACKETT. Those positions are for additional airport inspectors. There will be one in Chicago, two in Honolulu, one in Los Angeles, one in New Orleans, one in San Antonio, one in San Francisco, and one in Washington, D.C.

WORKLOAD AT NEW YORK AREA AIRPORTS

Mr. FOGARTY. Was the increase that we allowed last year sufficient for the workload in the New York area?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. That is not what I heard. Have you been up there lately?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. And they told you they were satisfied with the number of personnel they have there?

Dr. SACKETT. Sir, I might make the point that we have not as yet——

Mr. FOGARTY. They are not satisfied. If you do not know, I will tell you, because I have been there two or three times recently. They are terrifically overloaded with work up there. What did they ask? Did they ask for additional positions?

Dr. SACKETT. Yes, sir. They currently have a ceiling of 33 inspectors at Idlewild.

Mr. FOGARTY. Who provides this ceiling?

Dr. SACKETT. That is provided by the headquarters office from available positions and funds. I might say that we were not able to employ all of the inspectors which were authorized last year. You recall there were a total of 32 additional airport inspector positions, of which we were able to employ only 17.

Mr. FOGARTY. Why?

Mr. KELLY. Mr. Chairman, the Department had an overall limitation imposed of 3 percent reduction below the staff which could otherwise reasonably be financed. This reduction was to be applied against the absorption and the Pay Act costs, and the effect of this was to reduce the total authorized staff. The total reduction was not made against New York; but it did affect the staff in New York, so that the total authorized staff in the congressional action last year has not been achieved. The 1962 budget does contemplate achieving it.

Mr. FOGARTY. Well, what did they ask for for 1962? How many positions?

Dr. SACKETT. I believe the estimate that came to us was in the neighborhood of 63 positions.

Mr. FOGARTY. Now, how many does this budget allow for?

Dr. SACKETT. This will allow for 48 positions.

Mr. FOGARTY. What percentage cut is that?

Dr. SACKETT. Roughly 20 percent.

Mr. FOGARTY. That is quite a cut for a busy place; isn't it?

Dr. SACKETT. Yes, sir. We feel, however——

Mr. FOGARTY. You would not want to take it if you had charge, would you?

Dr. SACKETT. I do have charge.

Mr. FOGARTY. If you were located there in New York, you would not want to take a 20 percent cut, would you?

Dr. SACKETT. No, sir; I would not like it.

Mr. FOGARTY. Well, what happens when you cut an estimate like this by 20 percent?

Dr. SACKETT. Well, sir, we make increased use of overtime. During peak periods we do not allow annual leave. By measures of that sort, we are able to cover the peak workload.

Mr. FOGARTY. What do you mean when you say you do not allow annual leave?

Dr. SACKETT. Well, we encourage the men to take their annual vacations at times other than peak workloads.

Mr. FOGARTY. Well, there are other things that happen too. Why don't you tell me everything now?

If you don't have enough men, you don't do a good job. Do you want me to develop it for you? You know what happens when you do not have enough men to do a decent job.

Dr. SACKETT. Yes, sir. The funds we are requesting in this budget, with the restoration, will be adequate for us to provide minimum adequate coverage for our activity at Idlewild and the other airports.

Mr. FOGARTY. You mean the 48 will do a really good job, or just a medium job, or what?

Dr. SACKETT. Sir, the 48 positions are just for Idlewild.

Mr. FOGARTY. Doesn't Idlewild cover La Guardia?

Dr. SACKETT. Yes, sir; coverage is provided out of there but we also have a maritime activity in New York. I just wanted to make it clear that we were talking just about Idlewild.

Mr. FOGARTY. Will this require a lot of overtime and refusal of granting annual leave at peak periods?

Dr. SACKETT. Yes, sir. I believe this will be necessary with this number of positions. But not to an unreasonable extent.

Mr. FOGARTY. How many people do you think you would have to have to cut down overtime?

Dr. SACKETT. Well, any additional positions, of course, would reduce the amount of overtime that is required.

Mr. FOGARTY. Would you rather have more positions or more overtime?

Dr. SACKETT. Well, sir, we in general do not favor the use of overtime where it can be reasonably avoided. In places where we have peak load situations on a seasonal basis, it is difficult to avoid this and still maintain an economical operation. And we have attempted in this budget to achieve a reasonable balance.

Mr. FOGARTY. You are satisfied with the number of positions you are asking for for the New York area?

Dr. SACKETT. Yes, sir. For the budget year.

Mr. FOGARTY. The people up there are not going to like what you said, I am sure, if they read this record.

INSPECTORS REQUIRED FOR HONOLULU

For Honolulu you are asking for one additional position.

Dr. SACKETT. Two, sir.

Mr. FOGARTY. Do you think that is enough?

Dr. SACKETT. For the budget year; yes, sir.

Mr. FOGARTY. I came through there just recently. That is one of the busiest airports now, is it not?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. I have forgotten what increase they expect for the next year, but I thought it would take more than two positions out there.

Dr. SACKETT. They have gotten an increase recently of one inspector. We feel the additional two will cover their needs during the budget year.

It is increasing in activity.

Mr. FOGARTY. They expect a large increase of air travel through there during the coming year.

Do you think two additional men are enough to give adequate protection, good examinations, and so forth, or are you going to cut down on the service?

Dr. SACKETT. Sir, with the two additional positions we feel we will be able to provide minimum adequate coverage.

Mr. FOGARTY. What is the difference between minimum and good coverage?

Dr. SACKETT. Well, we feel that the number of positions that are required to provide minimum coverage are those that are necessary to meet our commitments so that there are no gaps in our program.

Beyond that level of coverage, personnel can be conveniently and profitably used to prevent the necessity for overtime and the necessity for discouraging annual leave at peak seasons, and so forth.

Mr. FOGARTY. I thought minimum coverage meant that it would leave gaps in your operations, and it would bring it down to a dangerous level of operation.

You don't agree with my interpretation of minimum coverage, do you?

Dr. SACKETT. I would not say that I disagree with you, sir. I would say that these increases which we are requesting are the amounts that have been arrived at through the budgetary process.

Mr. FOGARTY. Well, I am more concerned about what we need to do a good job. I expect you to give us your best professional answer, whatever that is, regardless of the budgetary process.

POSITIONS REQUESTED FOR 1962

What did you ask the Department for?

Dr. SACKETT. Our request of the Department was for an increase of 37.

Mr. FOGARTY. What did they ask the Bureau of the Budget for?

Dr. SACKETT. An increase of 17.

Mr. FOGARTY. The Department cut you 20 positions?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. Well, we cannot blame you very well. We have to blame the Department, then.

Dr. SACKETT. I would like to make this point, sir. Last year the Congress gave an increase of 20 positions over the President's budget. This occurred at a time that the preliminary estimate process was going on. So that by the time our estimate had gotten to the Department, the increase of 20 had already been provided by Congress for Idlewild.

Mr. FOGARTY. So they gave you what you actually requested.

Dr. SACKETT. Yes, sir; in effect.

Mr. FOGARTY. Then what did the Bureau of the Budget allow?

Dr. SACKETT. Eight, sir.

Mr. FOGARTY. They cut your request in half?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. Do you still think you could use those additional nine positions?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. Where would they be used?

Mr. RALPH RIGGS. Of the nine that were cut out, there was one at Anchorage, one at Honolulu, two at Los Angeles, four at Miami, and one at Washington, D.C.

Mr. FOGARTY. I was going to ask about Los Angeles and Miami. I thought they were shorthanded, too.

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. I was through Los Angeles about a month ago. They were really shorthanded out there. There is more business at Miami every year.

Dr. SACKETT. Yes, sir. The traffic has increased substantially. It does present difficulties in maintaining adequate coverage. Our increase for Miami requested of the Bureau of the Budget was four.

CRITERIA TO DETERMINE PAY COST ABSORPTION

Mr. FOGARTY. You had to absorb the increased pay costs. The National Institutes of Health absorbed it all, too, didn't they?

Mr. KELLY. Yes, sir.

Mr. FOGARTY. But in appropriation after appropriation in the Department of Labor and other parts of the HEW, they were not required to absorb a dime. Why do you pick on the Public Health Service?

Mr. KELLY. Well, candidly speaking, sir, there was an absorption in all of the appropriations except those that met a couple of conditions. One of these conditions was that the Secretary could exempt from the 3-percent reduction in staff those agencies engaged in direct medical care—the Hospital Division and the Indian health program. And he also exempted from the operation of 3-percent reduction those activities which were required to operate on a deficiency basis because of the enactment of new legislation.

Now, although I indicated that they were exempted from the 3-percent reduction, there were some instances where there was an absorption of the pay increase, such as in the Hospital Division, where although they were not required to decrease their employment by 3 percent, we had a savings resulting from the Manhattan Beach closure that permitted us to absorb part of the pay increase. So I do not believe the Public Health Service was treated any differently. We applied a single criteria to all the activities of the department.

Mr. FOGARTY. When these additional inspectors were provided by Congress last year, that was almost a mandate by Congress to provide these services. Then you say, "Well, we are not going to allow it." The Senate made it very clear in their report and the conference report spelled it out very clearly, we thought.

Mr. KELLY. Secretary Flemming was well aware of this. As a matter of fact, he indicated to the Public Health Service that in the application of the overall 3 percent, he did not want any discrimination made against an activity such as the Idlewild increase that had been provided by the Congress—that they share equitably in this reduction from the total positions that were authorized.

Mr. FOGARTY. Well, in the Department of Labor there are only four appropriations that absorbed anything. So I was wondering whether the formula was applied equally throughout the Government.

POSITIONS REQUESTED IN 1962

You still think you can use those nine positions that the Bureau of the Budget disallowed, Doctor?

Dr. SACKETT. Yes, sir.

Mr. FOGARTY. How much money would it cost?

Dr. SACKETT. We would be glad to furnish that for the record.

(The information requested follows:)

Cost of nine airport positions not allowed by the Bureau of the Budget—$94,000 of which $67,500 is for personnel compensation and benefits.

PROVISION FOR OVERTIME SERVICES BY CONTRACT PERSONNEL

Mr. FOGARTY. When I was in Puerto Rico, Doctor, there was a problem with inspection outside regular hours by contract doctors which I had the clerk call to your attention. Would you tell us what can be done about that?

It apparently is costing shippers a considerable amount of money because they have to lay out there for 3, 4, or 5 hours waiting for clearance. They were the ones that were raising this question.

Dr. SACKETT. Sir, provision of overtime services by contract personnel was not authorized under the terms of the Overtime Act.

The physician under contract provides services at an agreed upon rate—regardless of when he performs these services. If he wishes, he can provide them at night. But he is not obligated to do that. So there is this problem that is not really restricted entirely to Puerto Rico.

Mr. FOGARTY. Where else do you have this same problem?

Dr. SACKETT. Well, at several places where we use contract services. I recall one place on the eastern coast. I cannot think of the name of the port right now. We have such a problem at Key West, Fla., for example.

Mr. FOGARTY. Is there any way out of it?

Dr. SACKETT. Well, we have not been able to—we have explored the possibilities under the Overtime Act, and have been advised that it does not apply to contract, or should not apply to contract personnel.

Mr. FOGARTY. Is that spelled out in the law, or is that just in the regulations?

Mr. KELLY. The way the law was written, you recall that we were authorized to collect fees from shippers to reimburse us for the additional overtime cost paid employees by reason of providing the service in after hours. So that it is not a fee for service but it is a reimbursement for the cost that we incur by reason of the payment of overtime to our employees.

Mr. FOGARTY. So the law would not allow this either.

Mr. KELLY. It would not allow us to collect fees to perform this as an overtime service, after-hours service. We are not prohibited from providing the service, but we are prohibited from collecting a fee for rendering services over and above the normal services provided.

Dr. SACKETT. That is correct.

Mr. FOGARTY. Well, if Congress decided to appropriate a few thousand dollars for premium pay, would you then be allowed to pay these contract doctors?

Mr. KELLY. Well, I think we would, Mr. Chairman.

I would raise the question with you as to whether or not you would create an inequity if you required a shipper to pay a fee for getting after-hours service where we had employees stationed there and the work had to be done overtime, and did not require a shipper to pay when he got this extra after-hours service where a contract was involved.

Dr. SACKETT. I might say this, sir, that it is possible to draw up a contract that would permit an extra amount of money for services during overtime periods.

Mr. FOGARTY. Well, why don't you look into it? It seems to be a serious thing for a few shippers in that area.

Incidentally, Dr. Cashion is doing a very good job down there.

Dr. SACKETT. Yes, sir. He is.

YELLOW FEVER IN MEXICO

Mr. **Fogarty.** What is the situation in Mexico with regard to yellow fever?

Dr. **Sackett.** Sir, the Mexican Government, we have learned during the past year, through a meeting we had with the Health Minister of Mexico at Pensacola, has carried out quite an extensive *Aedes aegypti* eradication program, and also an immunization program. We were assured at that time that there was no yellow fever in Mexico during the past year.

SMALLPOX OUTBREAK IN MADRID

Mr. **Fogarty.** What about the smallpox outbreak in Madrid?

Dr. **Sackett.** Sir, a child entered Madrid, I believe on January 27 and became ill. The child came from Bombay, through Rome to Madrid. The child became ill, entered the hospital, and was diagnosed as having smallpox on February 6. We have since learned there are 15 secondary cases.

Mr. **Fogarty.** From that one case?

Dr. **Sackett.** Yes, sir. The original case died. We have not obtained any definite information as to the course that the disease has taken in the rest of them. We have learned so far of no further cases. I think the last case was reported to us around March 14.

Mr. **Fogarty.** But that is something you still have to be on the watch for all the time, is it not?

Dr. **Sackett.** Yes, sir. The countries that do not maintain a consistent program of requirements in this respect seem to have outbreaks of this sort on a fairly regular basis.

Mr. **Fogarty.** We have a lot of people from this country that go through these countries in a year, don't we?

Dr. **Sackett.** Yes, sir. More than any other country.

Mr. **Fogarty.** Where was this case headed for?

Dr **Sackett.** I believe the child was a resident of Madrid. That was the end of the voyage.

Dr. **Lowry.** This is not the flight map that has reference to that particular child, but this is another case that occurred in London. It shows the flight which originated in Hong Kong, and where it collected the people, and the smallpox that was present where they were. They got on the flight that went to London, and eventually ended up in New York.

Mr. **Fogarty.** There were 700 and some cases in Rio de Janeiro?

Dr. **Sackett.** Yes, sir. These are calendar year 1960 figures.

Mr. **Fogarty.** Nigeria, 329?

Dr. **Sackett.** That is in 1 week that was reported, yes, sir.

Mr. **Fogarty** 2,800 in Bombay?

Dr. **Sackett.** Yes, sir.

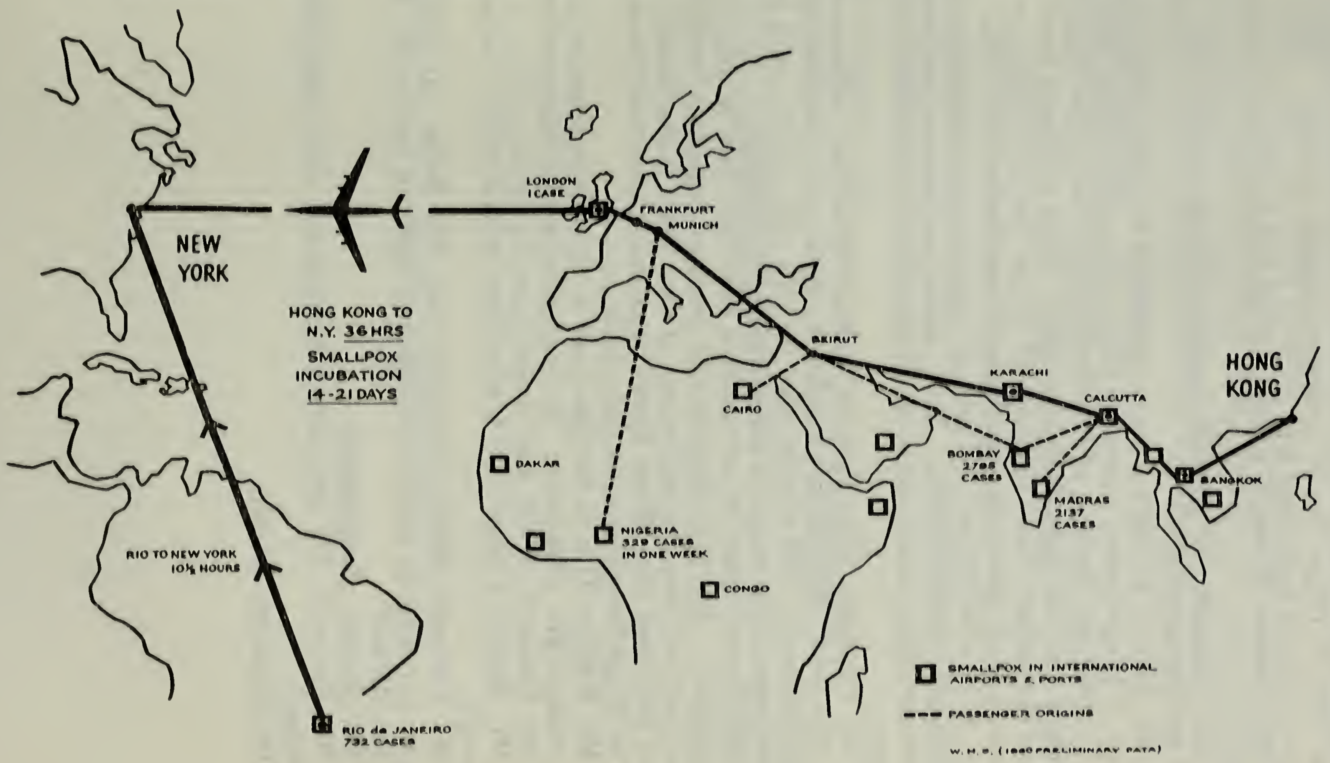
Also calendar year 1960.

Dr. **Lowry.** What we are trying to do is illustrate the reason why when you go to India we try to get you to be vaccinated before you go there, because we do not want anybody coming back to our country who will bring the disease with them. It takes 14 days to 3 weeks for the disease to develop, and, as you see, you can be exposed and be in the country for quite awhile before you get sick, if you happen to be nonimmune

(The chart being discussed follows:)

FLIGHT #1 and SMALLPOX

DEP. HONG KONG MON. OCT. 13, 8:30 P.M.
ARR. N.Y. TUES. OCT. 14, 7:30 P.M.



WAGE BOARD INCREASES

Mr. Fogarty. For both the medical services and foreign quarantine programs there are small decreases that are explained as "reduction in 1962 of Wage Board increases funded in 1961." That does not mean what it says, does it?

Dr. Lowry. I would like to ask Mr. Bahn if he can answer that one.

Mr. Fogarty. If you can make sense out of that one, you ought to get a promotion.

Mr. Bahn. In 1961 we are permitted to anticipate the full year cost of Wage Board increases which will occur in the year.

In 1962 the Bureau of the Budget does not allow funding in the budget year for those full year costs. They will only permit putting into the budget those amounts of Wage Boards which have actually materialized, generally up through September 15. This is part of the A–11—the Bureau of Budget circular on preparation of budget estimates—requirements. As a result, you have a reduction in the average salary anticipated for Wage Board employees in the budget year.

Mr. Fogarty. That does not make sense to me. You are an expert in this field. Would this not force you to go to the Subcommittee on Deficiencies? Did you fix this up this way so you will be sure to have something to go to them with next session?

Mr. Bahn. There is no question that this does in effect provide a deficiency. But then there would also be a deficiency in the following year anyway for annualization of the 1961 Wage Board increases, and for those new Wage Board increases that would occur in 1962. This Wage Board process has a built-in——

Mr. Kelly. This is not peculiar to this appropriation in our Department, Mr. Chairman. It is a governmentwide problem.

Mr. Fogarty. Well, does it make any sense to you?

Mr. Kelly. I must say I wish they would find a better way of doing it.

Mr. Fogarty. Well, you really tried, Mr. Bahn. It still does not make any sense to me, but I think you ought to get an "A" for effort.

Mr. Michel?

Mr. Michel. No questions.

Mr. Fogarty. Do you have anything else you would like to say, Doctor?

Dr. Sackett. No, sir.

HISTORY OF 1962 BUDGET AND USE OF ADDITIONAL EMPLOYEES

Mr. Fogarty. Would you be satisfied if you got those additional nine positions?

Dr. Sackett. Yes, sir. Very pleased.

Mr. Fogarty. Place in the record what you asked of the Department, what they asked the Bureau of the Budget for, and what the Bureau of the Budget allowed you. And give us a complete breakdown and narrative description—not just of international airport inspection, but your entire program.

Dr. Sackett. Yes, sir.

(The information is as follows:)

"Medical Care and Foreign Quarantine"

Foreign quarantine activities—Summary of changes

1961 foreign quarantine appropriation	$4, 931, 000
Comparative transfer to other accounts	—161, 200
Proposed supplemental for pay increases	179, 000
Total available in 1961	4, 948, 800
Allocated to program direction in medical care and foreign quarantine appropriation	28, 000
Available in 1961 for foreign quarantine activities	4, 920, 800
1962 estimate for foreign quarantine activities	5, 122, 100
Net change in activity estimate	201, 300

	1962 PHS request to Department		1962 Department request to Bureau of Budget		1962 budget estimate	
	Positions	Amount	Positions	Amount	Positions	Amount
For mandatory items:						
Annualization of new positions authorized in 1961	----------	$15,200	----------	$38,100	----------	$38,100
Increased cost of medical officers incentive pay for 1 year additional service	----------	3,800	----------	3,800	----------	3,800
Reclassification of sanitary inspectors and biological aids	----------	32,700	----------	35,200	----------	35,200
Annualization of 1961 pay increase and restoration of pay act costs absorbed in 1961	----------	106,000	----------	107,600	----------	107,600
Wage Board salary increases	----------	87,000	----------	65,900	----------	----------
Reserve officers retirement deducted in 1961	----------	6,000	----------	6,000	----------	----------
Subtotal	----------	250,700	----------	256,600	----------	184,700
For program items:						
Airport inspection program	37	294,700	17	[1] 190,600	8	64,000
Mexican border inspection program:						
Mobile X-ray units	4	54,900	4	61,100	----------	----------
Permanent X-ray equipment	----------	63,200	----------	38,300	----------	----------
Extended inspectional coverage at major crossing points. Positions located at Brownsville, Eagle Pass, El Paso, Hidalgo, and Laredo, Tex.; Nogales, Ariz.; Calexico and San Ysidro, Calif., and other objects related to these positions	16	105,900	----------	----------	----------	----------
Training of border inspectors. Positions of training officer and secretary and other related objects	2	14,000	----------	----------	----------	----------
Medical examination of visa applicants and epidemiological intelligence. Medical officer and aide positions in Japan, Mexico, and South America. Also included psychiatric and psychological screening staff of 2 positions to be located in Europe. Other object costs related to these positions are included	18	223,700	2	23,200	----------	----------
Strengthening headquarters:						
Position of field liaison officer; procedures writer; 2 secretarial and other objects related to these positions	----------	----------	4	33,600	----------	----------
Gross increases	77	1,007,100	27	603,400	8	248,700
Decreases:						
1 less day in excess of 52-week base (261 days in 1961, 260 days in 1962)	----------	10,600	----------	12,800	----------	12,800
Reduction in 1962 Wage Board increases funded in 1961	----------	----------	----------	----------	----------	20,300
Minor program changes	----------	800	7	14,300	----------	14,300
Subtotal	----------	11,400	7	27,100	----------	47,400
Net increases	77	995,700	20	576,300	8	201,300

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[1] The Department, in determining the 1962 allowance for the Division of Foreign Quarantine, considered the increase of the 20 additional airport positions provided by the Congress. These additional positions were added to the 1961 President's budget and in effect advanced the authorization for staffing at those airports most seriously undermanned because of increases in international traffic.

PROPOSED UTILIZATION OF ADDITIONAL PERSONNEL

Airport inspection program (*nine positions*).—The additional positions would be utilized to meet the increasing international traffic at the following airports: Honolulu (1), Los Angeles (2), Miami (4), Anchorage (1), and Washington, D.C. (1).

Mexican border inspection program (*four positions*).—Two mobile X-ray units containing 70-millimeter X-ray equipment are available. An inspection team consisting of one quarantine inspector and one X-ray technician would be assigned to each mobile unit. They would operate on a full-time basis to provide coverage at the crossing points not served by permanent X-ray installations.

Extended inspectional coverage at major crossing points (*16 positions*).—These positions would provide 24-hour quarantine coverage at the eight major border crossing points that receive the greatest portion of traffic from the interior of Mexico. With adequate 24-hour coverage at the crossing points with heaviest traffic, more than 95 percent of all traffic from the interior of Mexico would be covered. The additional positions would be assigned to Brownsville, Tex. (2), Eagle Pass, Tex. (1), Hidalgo, Tex. (2), Laredo, Tex. (2), Nogales, Ariz. (3), Calexico, Calif. (2), and San Ysidro, Calif. (4).

Training of border inspectors (*two positions*).—The additional positions of a training officer and clerk stenographer would establish and maintain a training program at El Paso, Tex., for quarantine activities along the Mexican border.

Medical examination of visa applicants and epidemiological intelligence (*18 positions*).—To meet the needs of this country in examining its prospective citizens and other aliens planning a prolonged stay in the United States, and to provide better intelligence concerning the worldwide occurrence of communicable diseases, additional staffing of medical officers, and medical aides would be utilized. The additional positions would provide staffing at Tokyo, Japan, Mexico City, Mexico, and Caracas and Buenos Aires, South America. Additionally two positions would establish a psychiatric and psychological screening staff to perform and supervise the mental screening of visa applicants in the entire European area.

Strengthening headquarters (*four positions*).—The addition of a liaison officer, a procedures writer and two clerical positions would strengthen the headquarters function in the areas of field supervision and the development of operating instructions and regulations.

Mr. Fogarty. Dr. Lowry, in conclusion now, do you have anything else you would like to add?

Dr. Lowry. No; except to thank you for your usual courteous hearing, Mr. Fogarty.

Mr. Fogarty. Dr. Terry?

Dr. Terry. I have nothing else, Mr. Chairman.

MARINE HOSPITALS

Mr. Fogarty. I have a few questions that I will give you and ask that the answers be supplied for the record.

(The information referred to follows:)

Question. It has been brought to our attention that research projects are being delayed because necessary structural changes are being held up. If this condition exists, at what locations, and what is recommended?

Answer. Structural improvements necessary for the conduct of research projects have been delayed at several of the hospitals including Boston, New Orleans, Seattle, and Staten Island. This delay is caused because of the deferment of administrative approvals for major capital improvements for the past 2 years, except those involving health and safety.

Question. It is claimed that little is being done to replace obsolete elevators, to set up an X-ray department where equipment already has been purchased, to install air conditioning in the hospitals where needed, and other similar items. Why are not improvements like these being accomplished?

Answer. Replacements of elevators, remodeling of X-ray departments, and other major capital improvements submitted as repair and improvement projects, require administrative approval. Excepting those projects involving fire and safety hazards, all approvals have been referred during the past 2 years.

Question. It has been reported that the Public Health Service hospitals generally are in serious need of capital improvements. What action is needed to correct this situation?

Answer. All of the Public Health Service hospitals are in need of capital improvements in the form of modernizations, improvements, or replacement. Preliminary plans have been developed for many of these but no significant capital improvements in general hospitals have been approved in the last 2 years.

Question. Some improvement in equipment has been made, but the need still appears to be considerable. Is it necessary to step up the equipment replacement program a little faster?

Answer. Considerable accomplishments have been made in reducing the backlog of equipment needs in our hospitals. A continuation of the program at the present rate should provide a reasonable equipment level in a few more years.

Question. The hospitals are reported to be short of help in some departments. If this is so, what is needed to correct this situation?

Answer. The 1962 budget, now submitted, includes a request for the fourth phase of personnel increases which, if approved, will provide staffing in the general hospitals at a level which was determined to be necessary when the program was started in 1957. Studies are now being conducted at individual hospitals, using workload requirements, to establish the staffing need for each activity of each hospital.

Question. We are informed that the University of Washington wants to set up a research program at the Seattle hospital beneficial to the Public Health Service. One floor of the hospital is available. However, Public Health Service funds apparently can not be used to relocate partitions so that the space could be utilized. What needs to be done in this instance?

Answer. Structural changes necessary for the establishment of a cooperative research program between the University of Washington and the Seattle Public Health Service Hospital will require administrative approval as a capital improvement. All capital improvements except those involving health and safety have been defined during the last 2 years.

Question. We have been advised that patients are required to wait unduly in the halls of many of the hospitals. What can be done to correct this situation?

Answer. This is an example of the serious overcrowding and congestion which can be corrected only by expansion and modernization of the present hospital buildings.

Question. We are advised that the Staten Island hospital has both hospital and office equipment in hallways. What would be the best solution to this problem?

Answer. Space deficiencies are prevalent at the Staten Island and other hospitals of the Service. Since original construction of the hospitals, there has developed a decided change in the pattern of patient care. Outpatient services have expanded enormously; laboratory, diagnostic, paramedical, and other services have demanded more space and have encroached upon other areas of the hospital resulting in overcrowding and congestion.

The only way in which this problem can be properly solved is through new construction and modernization of existing facilities.

Question. It has been reported that modern X-ray machines in the Staten Island hospital are being powered by temporary cables pulled in through windows, ceilings, or walls. What can be done to install and utilize this equipment efficiently?

Answer. It is true that temporary cables have been utilized to power the radiographic and fluoroscopic equipment, test treadmills, and other equipment which requires current in excess of what is available in the present cardiopulmonary laboratory.

This is an interim measure which has been adopted in order to avoid delay in carrying out a research project supported by a grant from the National Institutes of Health.

Permanent installation of equipment, laboratory benches, wall cabinets, and other improvements have been included in a repair and improvement project which has been submitted but for which administrative approval, as of this date, has been deferred.

Question. At Staten Island, it is reported that as many as five doctors are crowded into one room, toilet facilities carry four or five times the load they were meant to, and other facilities are equally bad. Serious overcrowding in some of the other hospitals was also reported. What can be done to relieve this problem?

Answer. There is considerable overcrowding and congestion in the Staten Island and other hospitals. Corrective measure would require an extensive modernization and improvement program.

Question. What are the ages of the various buildings being used by the Public Health Service on Staten Island and Manhattan? Could service in the New York area be improved if these apparently inefficient buildings were replaced with a modern unit in Manhattan?

Answer. The buildings and their dates of construction or acquisition are listed in the table below:

Staten Island:
- Hospital building: 1935.
- Nurses' home: 1935.
- Attendants' building: 1935.
- Boiler house: 1935.
- Outpatient building: Purchased 1837.
- Laundry: 1918.
- Quarters (8): Various (1909–19).
- Research building: Unknown (prior to 1900).

Manhattan:
- Outpatient clinic (Hudson and Jay Streets): Unknown (prior to 1909). Purchased from Society of the New York Hospitals, October 23, 1919.

The services in the New York area could be improved if the Public Health Service hospital were located in Manhattan. If original construction were being contemplated at this time, such a location should be given serious consideration, but the large capital investment in the present structures on Staten Island would make it more practical now to consider modernization and expansion at its present site.

The large outpatient clinic now located at Hudson and Jay Streets in Manhattan will move to the new U.S. Customs Court and Federal Office Building at Foley Square when it is completed.

UNOCCUPIED NURSES' HOMES

Mr. Fogarty. Last year we asked for a report on buildings in connection with your hospitals that are utilized less than 50-percent of capacity. We will insert the report in the record at this point and will expect that you have some plan worked out by next year to utilize these buildings.

(The report referred to follows:)

Department of Health, Education, and Welfare, Public Health Service, Hospitals and Medical Care

BUILDINGS OCCUPIED LESS THAN 50 PERCENT AND RECOMMENDATIONS FOR UTILIZATION OR DISPOSAL

House Report 1428, dated March 25, 1960, prepared by the Subcommittee on Departments of Labor and Health, Education, and Welfare and Related Agencies Appropriations, included a requirement that a complete report be submitted by December 31, 1960, concerning buildings owned in connection with Public Health Service hospitals that are being utilized at less than 50 percent of capacity.

Only two buildings were being utilized at less than 50 percent of capacity. These were two former nurses' homes, one at the Detroit, Mich., and the other at the San Francisco, Calif., hospitals. These buildings are vacant and have been totally unoccupied for more than 10 years except that from time to time they were used for temporary storage or for assemblies. The necessity for their use as nurses' homes which existed when they were built declined and shortly after World War II disappeared entirely for the following reasons: When the homes were built, the nursing staff of the hospitals was predominently a professional nurse group the majority of whom were unmarried. As time went on, the nursing work was reorganized so that the nonprofessional tasks were given to nursing assistants. These latter were recruited locally, and since they were already established in the community had no need for onstation housing. The professional group, too, began to include an increasingly larger proportion of married nurses, due in part from an increase in local recruitment as a source of staffing.

These factors have operated to reduce the utilization of the nurses' homes throughout the hospital system. Some are still in limited use (but exceeding 50 percent utilization), others have been converted to outpatient clinics, office space, interns' quarters, apartments, and other useful purposes. The information requested by the committee is supplied in two attachments as follows:

Location of hospital, building, and attachment with required information:

Detroit, Mich.—Nurses' home—attachment I.
San Francisco, Calif.—Nurses' home—attachment II.

ATTACHMENT I. REPORT ON UTILIZATION OF FORMER NURSES HOME AT THE U.S. PUBLIC HEALTH SERVICE HOSPITAL AT DETROIT, MICH.

I. DESCRIPTION OF BUILDING

The former nurses home is a three-story masonry building with a usable total area of 17,472 square feet.

II. CONDITION OF BUILDING

The building is in excellent condition except for deterioration of some of the plastering.

III. UTILIZATION AND COST OF MAINTENANCE

The nurses home at the Detroit, Mich., hospital has been vacant for the last 10 years. Portions of the building have been used for temporary storage from time to time and the building is occasionally used for assemblies. However, space is readily available for these purposes if a better use could be found for the nurses' home. Cost of maintenance has been at an average of $700 a year for the last 10 years.

IV. RENTAL RATES IN THE AREA AND POTENTIAL UTILIZATION IF BUILDING SHOULD BE CONVERTED TO QUARTERS

There is new rental housing in the immediate vicinity of the hospital which would be adequate for the staff but such units rent from $200 to $250 per month. Since such rates are far beyond what even the professional staff could be expected to pay, information was gathered as to the actual rentals paid by officers eligible for housing and the kind of housing that was being supplied at these rentals.

There are nine sets of quarters on the station now being occupied by commissioned officers. The remaining set of quarters has been assigned to a civil service physician who is a full-time employee of the hospital. Seventeen commissioned officers are eligible for quarters. Two of these were on leave when this information was obtained. Pertinent information was gathered from the remainder.

The situation of commissioned officers at the Detroit hospital who are eligible for quarters but are housed outside falls into three groups with varying needs. First, there are single officers without dependents; second are the single officers with dependents or married officers with no children or children under 2 years of age; and third are married officers with childen of school age. The housing situation of each of these goups is summarized below:

Unmarried officers without dependents

There are five single officers, two dentists, two nurses, and a dietitian. These have actual allowances ranging from $77 to $103 per month with the average at $91. One is housed on a room-and-board basis at $70 a month (but would take quarters if offered). The other four pay an average of $106 a month with the rental of each exceeding the allowance paid for quarters. These occupy one-bedroom apartments at an average distance of 9 miles from the hospital. North-south transportation to the hospital is not available so that at least one was "forced to buy an automobile," and one other had "no public transportation." Two of the rental apartments were described as substandard. Four of the five would take quarters if they were available.

Officers with dependents who are not children of school age[1]

This group contains six officers, three physicians, two therapists, and one dentist. Three have allowances of $103, the other three $120 per month for rentals. Apartments are rented to five of the six officers at a rental of from $120 to $125 per month, including the cost of utilities. The sixth pays $203 per month and is the only one who would not take quarters if they were available. All occupy two-bedroom apartments, and have the same transportation difficulties noted in the section above.

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[1] One single with dependent, two with children under 2 years, and three married with no children.

Married officers with children of school age

There are four married officers with children of school age. Three are physicians and one is a pharmacist. Three are allowed $103 and one $120 per month for rentals. One pays $160 for a two-bedroom apartment and two others pay $168 for three-bedroom apartments, including utilities. One of these latter has agreed to pay for such "minor repairs as may be required" in consideration of getting a lower rental. One of these officers, the pharmacist, pays $137 a month for a two-bedroom apartment. (He travels 20 miles each way daily.) He notes that rentals for housing to fit his needs are too high near the Public Health Service hospital. All would take quarters if they were available.

Voluntary hospitals in the area are building, or have built fully adequate quarters for their residents and interns. These installations find that they cannot attract and keep such staff unless they furnish such quarters.

V. RECOMMENDATIONS FOR BETTER UTILIZATION

In 1958, plans were developed by the station with Public Buildings Service assistance which recommended that the second and third floors of the nurses' home be converted into eight 2-bedroom apartments each with 1,000 square feet of living area. The south end of the first floor would be retained for station functions. The north end of the first floor would be converted to a laundry for the apartment occupants. The Public Buildings Service estimated cost for this conversion was $150,000.

This request was returned by the Office of Administration of the Department because the proposal did not appear to meet the general criteria for justification under administration policy as reflected in Bureau of the Budget Circular A-18 revised dated October 18, 1957, and because of the high cost estimate.

The pertinent policy which applies to housing for civilian or commissioned personnel as stated in Circular A-18 is quoted below:

"E. *Determination of whether construction is appropriate.* It is the policy of the Government not to provide housing for civilian employees except where necessary to maintain the continuity and efficiency of service, and in no case will the Government construct family housing for civilians or military personnel if private capital can be found to do the financing (either by privately financed Capehart military housing or by community support) * * *."

VI. CURRENT RECOMMENDATION

In response to the request for the information required by the subcommittee, the hospital again recommended conversion to quarters of the nurses' home as described above. No other utilization of this space is planned or anticipated. The net return to the Government from rentals, assuming a 4 percent rate of interest would amortize the cost of repairs in 36 years. The useful life of the building after conversion is estimated to be a minimum of 40 years.

The possibility of declaring the building surplus so that it could be used by some other agency had been considered but the only access is by passing between the other buildings of the hospital. This involves problems of access and control which make such a solution undesirable.

ATTACHMENT II. REPORT ON UTILIZATION OF NURSES HOME AT THE U.S. PUBLIC HEALTH SERVICE HOSPITAL AT SAN FRANCISCO, CALIF.

I. DESCRIPTION OF BUILDING

The nurses' home is a three-story building with basement. The building has a structural steel frame, reinforced concrete floors, brick walls, interior metal lath and plaster partitions and a hip roof with flat tiles. It has a usable floor area of 25,082 square feet.

II. CONDITION OF BUILDING

This building is in very good condition.

III. UTILIZATION AND COST OF MAINTENANCE

The nurses' home at the San Francisco, Calif., hospital has been vacant for the last 10 years. Portions of the building have been used for temporary storage from time to time and the building is occasionally used for assemblies. However, space is readily available for these purposes if a better use could be found for the nurses' home. Cost of maintenance has been at an average of $3,135 a year for the last 10 years.

IV. APPROXIMATE AVERAGE RENTAL RATES IN AREA

Average rental rates in the area for quarters similar to those that have been proposed in our recommendations for alterations are $125 to $175 per month.

V. RECOMMENDATIONS FOR BETTER UTILIZATION

It has been the station's recommendation since this building was declared inadequate as a nurses' home that it be converted into apartments, consisting of six 3-bedroom apartments, six 2-bedroom apartments, and six 1-bedroom apartments, drawings of which were prepared January 27, 1954, and submitted to headquarters. No action was taken by the Division of Hospitals on this request because it could not possibly be financed within the total of funds then available for such projects.

The possible use of this building for regional offices was considered for a time in 1954 but it did not appear to be suitable for that purpose.

This project was again proposed in connection with the feasibility survey conducted at this hospital, dated November 4, 1958, and was considered feasible by the architects conducting the survey. The feasibility survey was a total statement of construction needed to carry out fully the mission of the hospital. Copies of the surveys were forwarded to the Office of the Surgeon General and the Office of the Secretary. No action was taken because the funds required for the total construction were far beyond available resources.

On March 14, 1960, the Division of Hospitals forwarded the request again to the Public Health Service Division of Administrative Services. On May 8, 1960, a set of questions was raised in order to develop appropriate justification for the request. These were answered in a memorandum on June 22, 1960, which submitted a cost estimate by Public Buildings Service of $254,650 for the construction. A calculation was also submitted that showed that the cost of repairs would be amortized in 23 years assuming a 4-percent rate of interest. The life of the building was estimated at 40 years.

On July 22, 1960, a final submission of all major repair and improvement projects for fiscal year 1961 was made reflecting reductions of previous requests to come within funds to be made available. The conversion of the nurses' home at San Francisco was one of the projects deleted. It has not been considered advisable to implement this project to date because it has not met the criteria established by the Bureau of the Budget in Circular A–18 revised, dated October 18, 1957, which is quoted under the portion of this report pertaining to the Detroit nurses' home, and because requirements of greater urgency have taken up available funds.

Until quite recently, no other utilization of this building was planned. However, the Chief of the Division of Dental Public Health and Resources under date of November 29, 1960, presented a proposal to utilize part of this building to establish a field center to be devoted to applied and clinical research demonstrations and training. His plan contemplates inaugurating this field center in July 1961, should his proposal be favorably acted upon.

The space to be occupied in the first stage of setting up such a field center would require only refurbishing for immediate use. This and the equipment required, office furnishings for the most part, can be provided from funds already available for that purpose. Any substantial additional requirement for altering or equipping such a field dental center would be made the subject of a future specific request for funds.

The San Francisco area is ideally suited for this and other research purposes because of the availability in the area of a major university, a medical school, a dental school and a school of public health. The utilization of the nurses' home building for conversion to research facilities (dental and other) will be more advantageous to the overall program of the Division of Hospitals than utilization of the building for quarters for staff.

This proposal is currently under consideration in the Public Health Service and a decision is expected shortly.

WEDNESDAY, MARCH 22, 1961.

NATIONAL INSTITUTES OF HEALTH

WITNESSES

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DAVID E. PRICE, DEPUTY DIRECTOR, NIH

DR. G. BURROUGHS MIDER, DIRECTOR OF LABORATORIES AND CLINICS, NIH

RICHARD L. SEGGEL, EXECUTIVE OFFICER, NIH

DR. LUTHER L. TERRY, SURGEON GENERAL

HARRY L. DORAN, CHIEF FINANCE OFFICER

DR. HALSEY HUNT, CHIEF, DIVISION OF GENERAL MEDICAL SCIENCES

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Mr. FOGARTY. The committee will come to order. We have before us this morning the National Institutes of Health. Do you have a statement, Dr. Shannon?

Dr. SHANNON. Yes, Mr. Fogarty, I have a statement.

GENERAL STATEMENT

Mr. Chairman and members of the committee, it is always a pleasure to appear before this committee to lay before you some of the considerations which underlie the Public Health Service's appropriation request relating to the programs and activities of the National Institutes of Health.

The thorough and understanding consideration which you have given our previous requests and the forthright and farseeing manner in which you have acted on them are deeply appreciated not only by my colleagues and myself but by the scientists and the institutions whose research work is, in large part, made possible by the generous support you have made available to them through the National Institutes of Health appropriations. This gratitude, I am sure, is also shared by the people of this country who are the ultimate beneficiaries of everything the National Institutes of Health do.

They have repeatedly shown themselves willing to finance—not only with taxes but through substantial voluntary contributions—a concerted and accelerating drive against the diseases, disabilities, and physical discomforts to which man has always been prey.

They have shown that they regard health research and its related activities as a matter of prime personal concern and as a great national need. The members of this committee—and, indeed, of the Congress as a whole—may well take pride in their bold and ready response to this need.

CHANGES IN TOP MANAGEMENT AT NIH

The expanding scope of the NIH programs and the qualitative changes brought about by the substantial increases that Congress has made in our appropriations during the past several years are reflected in our recent reorganization and diversification of the top management of NIH.

We are fortunate to have, as Deputy Director, Dr. David E. Price, who is here today. Dr. Price has had wide experience in the Public Health Service in which he has been a commissioned officer for the past 20 years, having served successively as Associate Director of NIH; in the Office of the Surgeon General; as Deputy Chief of the Bureau of Medical Services; and as Chief of the Bureau of State Services. He has now returned to NIH to assume primary responsibility for the research, research training, and research facilities construction programs.

The intramural research programs are under the general direction of Dr. G. Burroughs Mider, who left his post as Associate Director of the National Cancer Institute in order to take the newly created post of Director of Laboratories and Clinics. Dr. Jack Masur continues as Director of the Clinical Center with the additional title of Associate Director for Clinical Care Administration.

Dr. Ernest M. Allen has relinquished his operating responsibilities as Chief of the Division of Research Grants to devote full time to policy and broad administrative problems as Associate Director for Research Grants.

Our concern with the impact of NIH programs on grantee institutions, about which I want to speak in a moment, is such that it has become the special province of a senior member of the NIH staff. Dr. Charles V. Kidd, who has long had a keen interest in the impact of Federal programs on universities and other institutions and who has for many years been Chief of our Office of Program Planning, has been appointed Associate Director for Institutional Relations with broad responsibility for the development of such newly emerging programs as institutional grants, research-center grants, and career research professorships.

In addition to these new positions, the plan for the reorganization of the senior staff envisages an Associate Director for Training. Filling this position has, however, been temporarily deferred pending clarification of the extent to which NIH's role in this area should properly be expanded both in the light of the administration's plans for more comprehensive aid to higher education, and of a reassessment by NIH—to which I will revert later—of the proper balance in its training programs.

EXPANSION OF THE BETHESDA CENTER

The growth of NIH activities is also reflected in the physical appearance of the campus in Bethesda. The building for the Division of Biologics Standards, which the King of Thailand graciously dedicated last June 30, has enabled us to bring that Division under one roof for the first time in its history with obvious benefits to its programs.

The building for the National Institute of Dental Research will be dedicated at the end of May and will be fully occupied by late summer. The completion of this well-equipped laboratory building will pave the way for further developing research in this very important field.

Good progress is being made in the preparation of plans for the new building to be shared by the National Institute for Neurology and Blindness and the National Institute for Mental Health, which the Congress authorized last year; and in developing the program requirements for the new building for the National Cancer Institute, for which planning money was appropriated.

The modern surgical wing for the Clinical Center is expected to be ready this fall. It is, we think, a model of careful design to meet the specialized requirements of heart surgery and for the study of brain tumors, stroke, epilepsy, and other neurological disorders.

SPACE PROBLEMS

The new administration building will also be completed by the latter part of this year. I might say we expect to move into part of it late this summer, but full occupancy will have to be deferred until later in the year. Its 173,000 square feet of office space will enable us to bring together the sections of the several Institutes concerned with the operation of the grant programs as well as to accommodate in a central location six of the Institute Directors and their immediate staffs. An additional important benefit of this construction is that it will allow us to return space in other buildings to the research use for which it was originally intended. However, the increase in staff resulting from the rapid expansion of NIH programs, during the 3 years that have elapsed since this building was designed, has been such that our requirements—even before the building is occupied—already exceed its capacity. It will therefore, unfortunately, not yet be possible to bring to the NIH campus all of the sections of the Institutes now scattered in half a dozen buildings in Bethesda and Silver Spring.

We estimate that we shall have to continue to house about 1,000 employees in rented space in 1962—and this, of course, does not take account of possible expansion in the future. This geographical dispersion entails serious functional and administrative problems. Communication difficulties, transportation delays, and subtle effects on the morale of the off-campus staff make more difficult the close and constant teamwork which is essential to the smooth operation of a complex organization.

Lack of suitable space has already deterred us from hiring staff for tasks which might contribute to the efficiency of our operation and it has interfered with the proper functioning of some sections for which it has not been possible to house the entire staff in one place or which have not had room for the large pieces of equipment that could greatly facilitate and expedite their work. I therefore hope that this committee will act favorably on our request for $700,000 for the planning of an additional major office facility.

Mr. FOGARTY. Is that a budgeted item?

Dr. Shannon. Yes, sir. That is in the general appropriation of the Public Health Service for construction. This was presented as an overall item immediately after Dr. Terry's introductory testimony.

Mr. Fogarty. I think you had better give us for the record the status of the other building projects so we can get them all in one place.

Dr. Shannon. That are in the budget, sir?

Mr. Fogarty. Those that are in the budget, and those you asked for and didn't get. Give us a brief explanation of each.

Dr. Shannon. I can outline this just briefly and give you a brief summary, then if you wish to inquire into any one of these, I would like to look to the help of Mr. Seggel or Dr. Mider.

Mr. Fogarty. All right.

CONSTRUCTION BUDGETED IN 1962

Dr. Shannon. In the present budget there is a request for the National Institutes of Health farm of $2,800,000. This is for building some of the initial structures, and for planning and providing some of the general utilities. There is an item of $700,000—to which I just spoke—that represents the cost of planning the second administration building.

Mr. Fogarty. Do you think that will be big enough?

Dr. Shannon. That building is planned, tentatively, to house 1,400 people. We feel that this is as large a building as we can plan for the best site on the reservation that it will fit; namely, in close juxtaposition to the administration building now being built. We would occupy this during the coming year. This would provide us with space for growth between now and completion of the building for some 400 people.

While I don't believe that this additional facility would satisfy any long-range projection of what our need is, it probably would satisfy our immediate needs. We feel that it is difficult to predict what the administrative load of the National Institutes of Health will be, looking forward to perhaps a 10-year span of program development. But we undertook a serious study——

Mr. Fogarty. It could be in the billions.

POSSIBLE DECENTRALIZED OPERATION

Dr. Shannon. Yes, sir. But we feel that if we go to another order of magnitude, it is quite likely that our programs would be better administered if we decentralized certain of the operations.

For example, in California our total programs amount to approximately $30 million. I think that it would be well worthwhile—and in fact we are now considering whether it would not be wise—to put a staff in residence in San Francisco to cover the activities of NIH in relation to institutions in the California area.

We made a survey of the activities in the Boston area and they amount to—I recall the figure in grants alone being something in the order of magnitude of $30 million. It is quite conceivable that a similar thing should be done there.

In fact, we may be approaching the point, as happened many years ago in the large contract programs of Defense, where we have to have the equivalent of resident engineers—who, in our case, would be resident extramural staff—to service grants locally and to minimize the number of small decisions that have to be made centrally so that the top staff that remains in Bethesda can be more concerned with the broad decisions than with the followthrough of their implementation.

This is a very sizable step away from our present concept of grant administration. In the course of the coming year we will probably try, in one or, perhaps, in two institutions, to see what can be done by such a decentralization process and to see if we should work out, over the years, the establishment of peripheral administrative units. In that case we would need more space in the future, but we would not need to centralize all office procedures within a single installation.

I think this is a worthwhile thing to look into, sir.

Mr. Fogarty. Could that be construed as Federal aid to medical education?

Dr. Shannon. No, sir; I don't believe so. It would mean that we would house auditors and program directors in close association with the dollar activities they supervise; but this would in no way put us in any different position, relative to the institutions that receive support from our funds, than we are actually in now.

FEDERAL SUPPORT OF MEDICAL EDUCATION

Mr. Fogarty. If in the next 10 years the grants to these medical institutions increase as much as they have in the last 10, that would be aid to medical education in a pretty substantial way, wouldn't it?

Dr. Shannon. I would say, sir, that Federal aid to education—medical education—does not bother me at all. I believe that for many years we are not only going to have Federal aid to medical education, but that this is essential for the sound development of our educational institutions.

As you know, the Department has submitted, in parallel with the bills you have submitted, certain proposals whereby a beginning can be made in this very difficult area.

Mr. Fogarty. Which one do you think is best?

Dr. Shannon. That is a difficult question for me to answer in this sense, Mr. Fogarty, that the proposals——

Mr. Fogarty. I won't press you for an answer to that.

Dr. Shannon. Mr. Fogarty, the present administration proposes certain elements that you are proposing, sir. I might say that we have not been designated as the responsible agency within the Public Health Service to administer or defend the proposals that have been made. I would be loath to go into this in detail.

Mr. Fogarty. Who is the——

Dr. Shannon. At the present time this is being dealt with by the Office of the Surgeon General, sir. I am sure they have detailed information that is not available to me, and they would be in a position to make much more accurate comments than would I.

Mr. Fogarty. All right, you may continue with your statement.

CONSTRUCTION AND ALTERATIONS AT THE BETHESDA CENTER

Dr. SHANNON. We have a very serious problem in the utility services at Bethesda. It is perfectly obvious that we have to stop now and redesign the basic utility system that was originally designed for a small complex of buildings and provide the flexibility that will make it possible to develop in the future. If we don't do this, each new increment of enclosed space we put on the reservation will cost an inordinate amount for utilities.

There is an item in the budget for the design, planning, and development of a master utility plan in the amount of $645,000. There is an item of $85,000 in the animal breeding area in Bethesda, and there is an item in the present 1961 budget to renovate and rehabilitate two areas.

I think the specifics of this Dr. Mider probably has.

Mr. FOGARTY. All right, we will ask him for the information later.

Dr. SHANNON. This is an extension of a plan that was begun this year. It was the judgment of the Bureau of the Budget that we defer completion of the first stage of the farm development, which we had asked the Department to support to the extent of $1,195,000, and that we leave to the Public Buildings Administration the obtaining of funds for repair and improvement amounting to $1,392,000. This, as you know, Mr. Fogarty, is a service that is provided by the Public Buildings Administration for all Government agencies. We proposed—and, I believe, with the strong support of the Department—that, because our capital investment was so large, they should, perhaps, depart from this convention in this particular case. But we have been assured that this is not desirable on a governmentwide basis, and we are hopefully looking forward to adequate attention to this through the normal routes of administration.

Finally, we requested funds for the extension and enlargement of Building 12, which would house the new computer setup and permit us to bring many of our office functions related to payroll and accounts into close relationship to the machines that service them.

Those, then, sir, are the items that are in the budget and the items in our initial proposal to the Department which were found to be, in the best judgment of the Bureau of the Budget, deferrable items—five in one category and three in the other.

I would be glad to discuss any one of these items—with the help, as I say, of Dr. Mider and Mr. Seggel.

Mr. FOGARTY. Why was this addition refused to house these computers? Don't you think it would save money in the long run to go ahead with it?

Dr. SHANNON. We think, sir, that this is an essential part of the evolution of the program. We hoped that, if we submitted it this year, it would be accepted. We know we have the support of the Department for this item. This was one of the items that fell by the wayside when the budget was adjusted.

Mr. FOGARTY. Do you think we would save money if this was allowed?

Dr. SHANNON. Yes, sir; I think we would. It would do two things: One, we would have a better operation, which in itself saves money, in that we would have adequate facilities for the new computer setup and, two, we would have the offices which use the computer localized in a single space and close to the computer iteslf. There would be a saving of money plus a much more efficient operation. I don't think you could point to the fact that by doing this now we could take many positions out of the budget; but I think, simply, that we could do a better job and I think we could do more things. In this sense it would be a saving.

Mr. FOGARTY. All right, go ahead.

INTRAMURAL RESEARCH

Dr. SHANNON. In view of the dramatic changes in the scope and direction of the NIH grant programs, much of this overview of our activities must necessarily deal with the extramural component. This should not, however, be allowed to obscure the fact that NIH began as, is now, and must continue to be, primarily a research institution of acknowledged excellence, imagination, and drive.

Not only does the public, in return for its unstinting support, have a right to expect a vigorous research program of the highest quality; but such a program is, in fact, an essential prerequisite for the successful operation of the extramural programs that now sustain so significant a proportion of the Nation's total medical research effort. NIH occupies a position of leadership in the scientific community not just because NIH makes available to it much-needed funds, but because the judgment of the NIH professional staff is accepted as reflecting the broad scientific experience and achievement of a respected peer group.

I should like to underscore the importance of our onsite research by mentioning, very briefly, a few examples of work done at NIH. Recent progress reports include:

MALARIA STUDIES

(1) The discovery that simian malaria can be transmitted to man by the bite of an infected mosquito, indicating that there may be hitherto unsuspected sources from which humans may be infected by new strains of malaria parasites.

Mr. DENTON. May I just ask, how is that different from what we know now? We knew mosquitoes carry malaria.

Dr. SHANNON. This has a profound effect on the most important single program undertaken by the World Health Organization; namely, the eradication of malaria. Until recently the belief has been that malaria existed only in the mosquito, which infects man, and that if one could interrupt the chain between mosquito and man, one could eradicate the disease.

It now turns out that malaria is more like yellow fever. In addition to the mosquito-man relationship—there is a mosquito-monkey relationship, which means that in the jungles around the world, which is the broad malaria reservoir, the interruption of the mosquito-man relationship will in no way eradicate the disease.

In other words, this is very similar to yellow fever. We have the ability to interrupt the mosquito-man relationship in yellow fever; but there is this large reservoir of jungle yellow fever that is spread all over Africa, and a good part of South America, that precludes removal of the disease from these areas.

This means that the total control program must now be reassessed because there is this unsuspected reservoir that can contribute to the spread of the disease. As one eradicates it in man, the reservoir will continue to feed it in.

Mr. DENTON. You mean monkeys and other things like that have malaria, too?

Dr. SHANNON. Yes, sir. It has always been known that monkeys had malaria. But the pertinent finding during the past year is that the species of malaria that have heretofore been thought to be peculiar to man are not peculiar to man but are common infectious agents for man and monkeys.

So, you see, this changes the whole problem. During the past year there has been a reassessment. We now have to take the next step and determine whether this reservoir, in fact, maintains a high level of epidemic disease or contributes only to a very slight extent. If it contributes to a very slight extent, it will be possible—still using the techniques we are using now—to suppress malaria substantially without eradicating it.

But if the interchange between man, monkey, and mosquito is rapid, then the problem of eradication in many areas is hopeless. Applying known engineering techniques to a disease problem is seldom successful unless all the necessary knowledge is available. It turns out in this case, that this was an essential piece of knowledge that was not available when the original programs were developed.

DENTAL CARIES

(2) Evidence, from studies of germfree animals, that a specific micro-organism may be the cause of dental caries, with the implication that immunologic or chemotherapeutic prevention may be possible.

Mr. Denton, what I might do is point out the Institute involved here. If you have a particular interest in any one of the problems, it will be possible for the Institute Director, as he comes up, to bring a short, capsule summary that will have been thoughfully prepared and will sound better, perhaps, than my extemporaneous comment. This obviously is a contribution of the Dental Institute.

ATHEROSCLEROSIS

(3) The discovery (in animal studies) that the interplay between the rates at which cholesterol—this is the fatty substance that causes atherosclerosis—enters and leaves the wall of major arteries is a significant factor in the development of atherosclerosis. In other words, this is not a static deposition of fat which, once deposited, is permanently a residue in that locus. There is an interchange of fat going in and out. The factors that determine the rates of this interchange determine the amount that is retained and this, in turn, determines the development of the disease.

The important thing about this discovery is that, having demonstrated that this is completely reversible, then the introduction of curative therapeutics, at a later stage, will have a profound effect on the progress of the disease. This is very important, because atherosclerosis as a disease entity begins in man in the late twenties but does not begin to cause serious trouble until the fifties.

If this is an irremediable defect by the time one enters the fifties, then one can do nothing about it. And the attempt to develop curative methods would not be a very profitable enterprise. But if the process is reversible, curative methods can conceivably be developed and used to control this disease with profound social and economic effects.

NEUROVIRULENCE OF TYPE 1 POLIO VIRUS

(4) Evidence that the infectivity and neurovirulence of type 1 polio virus is determined by the ribonucleic acid (RNA) of the virus. These viruses are composed of two general types of proteins. The ribonucleic acid is a nucleic acid that is found in viruses containing protein that determines many characteristics. This is now separable as a virus entity for study. This is very important and has ramifications all up and down the line, including the development and use of a live polio vaccine—because here, if one can be sure, as we are, that neurovirulence is resident in the organism because of the type of this particular nucleic acid, we have available a means for studying and controlling the neuro-infectivity of normal live polio vaccine.

It puts the control in the hands of the chemist rather than in the hands of a very complex biological study group involving extensive use of monkeys.

DRUGS AFFECTING THE NERVOUS SYSTEM

(5) The development of a rapid chemical method for measuring the activity of the enzyme, montamine oxidase, which is of central importance to our understanding of a wide variety of phenomena related to hypertension and mental disorders, as well as of the mechanism by which drugs can modify these disease processes.

Again this is a long step forward in the understanding of how blood-pressure-lowering drugs work. And how drugs affecting the central nervous system work. With better understanding, they will become more effective agents.

CHEMOTHERAPY OF UTERINE CHORIOCARCINOMA

(6) Continued encouraging results in the chemotherapy of uterine choriocarcinoma with massive doses of methotrexate; of 63 women treated at the Clinical Center, 30 have by now been in complete remission for at least 1 year, while several have remained free of all evidence of disease for 5 years. Early diagnosis appears to be the most critical determinant of the success of treatment.

Here you have, for the first time, a clear demonstration that a chemical agent can, in fact, cure cancer. This is not a cure by surgical means; nor is it destruction by radiology. It is a cure by a chemical agent in much the same way that you can cure a bacterial disease by penicillin or streptomycin. This is a very dramatic advance.

These examples, Mr. Chairman, are random selections which do not necessarily represent the most significant advances along the broad front of our investigations. I could as easily—and with more justice to our scientists—have cited 60 as 6.

PROBLEMS OF HOLDING PROFESSIONAL EMPLOYEES

In order to maintain the high level of accomplishment which has come to be expected of the NIH staff—in terms both of the quality of their work and the broad range of their research interests—it is, of course, essential that we continue to attract scientists of the highest caliber. This is no longer as easy as it was, even a few years ago, when NIH could offer unmatchable facilities for research; a uniquely stimulating research environment; and pay scales which, in relation to those of most academic institutions, were at least competitive.

It is a measure of the success of the NIH grant system that equally good facilities, equally vigorous research programs and, in some cases, better remunerative arrangements (which often include opportunities for private practice or consultation) now exist at many of our medical schools, universities, and teaching hospitals.

I am sure you will agree that this is a development which the people of this country will applaud because it means that there has been a very marked increase in our total national research potential in the biomedical sciences. But it is a development which now makes the task of the scientific directors of the various institutes, who are responsible for staffing the NIH laboratories, a frequently frustrating experience.

We are now losing too high a proportion of our truly exceptional scientists to other institutions that can—and do—entice them with sometimes irresistible inducements. It clearly behooves us not to let concern with the manifold administrative problems of a rapidly evolving extramural program divert us from a constant, watchful preoccupation with the maintenance of the most propitious conditions for scientific excellence on the Bethesda campus. These conditions must include excellence of research facilities, intelligent and considerate administration, due recognition of achievement, opportunities for promotion, and pay scales that will not only withstand comparison with those of the better universities but will to some extent offset the opportunities for supplemental income which attend most university appointments.

Mr. Fogarty. We have been talking about your personnel problem at the institutes for some years now; but we are not making much headway. Do you have anything you would like to add to your statement? I know you have been discussing it for some time.

Dr. Shannon. Mr. Fogarty, this is what I take to be not only a serious problem but a critical problem. I am very glad to report that in discussions with the Surgeon General and the Secretary we have had sympathetic understanding from both.

Mr. Fogarty. Sympathy isn't going to do you any good unless you get some action.

Dr. Shannon. To go beyond that, we have submitted to the Surgeon General—and I believe he has approved—a program that would do two things. One, it would increase the incentive and the pay scale for our scientists who are within the civil service system. Two, it would permit the detailing, for temporary periods, of a commissioned officer to a job that had been established at a given pay level without interfering with his long-term benefits under the Career Compensation Act of the military. It would permit him to obtain a more reasonable compensation for his services.

The critical nature of this perhaps, Mr. Fogarty, can best be explained if I give you an example of what has happened in one of our institutes. In order to save embarrassment to the individuals concerned, I should, perhaps, not identify the Institute or the individuals.

In an area in which we were intensively concerned to develop strong leadership, as part of our direct operations, we programed our resources so as to place primary dependence on four really topflight scientists.

Last summer three of the four were offered other posts. These were distinguished positions in our best universities, and two of the three accepted.

Mr. FOGARTY. What were they getting here and how much are they going to get where they are going?

Dr. SHANNON. They were getting $19,000 here, which is the top of our pay scale. The least any one of them will now get by going to the universities is $25,000—with an opportunity to conduct a part-time practice or do consulting work, or $30,000 to $35,000.

These, you will understand, Mr. Fogarty, are the top scientists in these areas in the country.

Mr. LAIRD. Dr. Shannon, it is probably true, though, that these schools and universities wouldn't be able to pay them the $25,000 and $30,000 if it wasn't for the training grants that you are making to the schools.

Dr. SHANNON. This was the point, Mr. Laird, that I made. We are very proud that we have been able to participate in the elevation of positions in our universities to a point where senior scientists can get sufficient remuneration to lead a life of some dignity and to educate their families and provide in some small measure for their future.

If, in providing this, we have undercut our own ability to conduct an effective operation, I would say that, on balance, we still have done a good job; and if we could do it over, we would do precisely the same.

I think we have come to a point now where we have to look inside as well as outside. Coming back to these four people, the third person has remained. But the university that was rejected by the third person immediately moved over to the fourth and took him. So of the top leadership in one of our Institutes as designated by us some 3 or 4 years ago, we have lost three out of the four leaders within a period of 6 months.

To give you another example, we established some distinguished lectureships for our intramural personnel approximately 2 years ago. These are two a year for our most distinguished scientists. As this is the second year, there have been four such lecturers. Two of these four have now accepted posts in universities.

Well, sir, we cannot afford to lose this type of personnel at the rate we are losing it. I realize it may be of concern to this committee, but this is not the place for us to make our case. But I would hope that if these proposals come to the Congress for discussion we can give you some inkling of the factors that cause this difficulty and we would hope that you would give them vigorous support.

Mr. FOGARTY. This may not be the place to state the case, but we would like to know if you are making any headway, what you have done and what legislation has been prepared and what the status of it is.

Dr. SHANNON. I would be glad, if you wish, to make a report on that available to you. At the present time our proposals, as I have stated, are much more extensive than I have described to this committee. They are now, I understand, in the Surgeon General's office, and he agrees in general with our conclusions as to the need.

But I believe that he is trying to determine where they fit in terms of the overall needs of the Service before he presents them to the Secretary.

Mr. FOGARTY. I think the Secretary said the same thing when he was speaking to this problem; but all the sympathy in the world isn't going to solve it. Dr. Terry, what is the status of this problem now?

Dr. TERRY. Dr. Shannon has stated it quite accurately. He and I have had discussions with the Secretary relative to the problem. However, at this time no specific proposals have gone to the Secretary from the Public Health Service.

Mr. FOGARTY. When do you expect they might?

Dr. TERRY. Very soon, sir.

Mr. FOGARTY. Do you hope to get something before Congress this year?

Dr. TERRY. We would certainly hope to, sir.

POSSIBLE SEPARATION OF NIH FROM PHS

Mr. FOGARTY. Let me ask you this question which I asked Secretary Ribicoff and the Surgeon General. What would you think about divorcing the NIH from the Public Health Service and setting it up as a separate agency?

Dr. SHANNON. In the first place, Mr. Fogarty, I should say we are probably the last ones who should be asked such a question because we are the ones most intimately concerned with the answer and therefore probably tend to approach this in a very subjective way.

I would point out that we have flourished under the present administrative arrangements, and I think that we can look forward to flourishing in the future. I think the question you propose relates to the function of the Surgeon General's office to determine how the overall functions of the Public Health Service can best be handled, and to the Secretary in terms of whether he feels that programs of this size and complexity are sufficiently sensitive to the political direction that must come from his Office. And, in fact, it is of importance to the President's Office itself in connection with his development of a sound science plan for the Nation.

One can view medical research and education as a thing in itself; or one can view it as part of a total health pattern. One can also view it more in relation to education, in which case it is more closely allied to the educational function of the Department. Or one can view it as a part of the fabric of science, in which case it is more closely allied to the National Science Foundation.

I might say, Mr. Fogarty, that this subject was seriously discussed by the National Science Foundation committee that looked at our operations—I believe, in the summer of 1956; and by the Bayne-Jones committee which considered this problem in 1957 and 1958; and by the recent committee of Senate consultants who looked at our programs during the last fiscal year.

Mr. Laird. What about the Cohen committee? Did they get into that?

Dr. Shannon. They didn't get into it, sir. The general decision there, after much—I would say—detailed consideration, is that there were arguments for and against. But on balance, they felt that the NIH had flourished where it is and that the disruption that would be caused by separation would, in the aggregate, have more unfortunate than beneficial consequences.

Mr. Fogarty. I don't want to embarrass you or the Surgeon General either. I just asked the Secretary the other day. That is the first time I ever asked the question. He hadn't given it much thought and didn't know it had been studied.

I can see where the NIH flourished under the Public Health Service, and I can see where the Public Health Service has been helped tremendously by the establishment of the Institutes of Health.

I don't know if they need to depend on one another at this point.

Dr. Shannon. Mr. Fogarty, I think this is a question of some significance. I would say it is a question that perhaps one should return to at times. There is much talk today about the organization of science in Government.

There are certain suggestions that will emerge from the National Science Foundation's period of self-inquiry during the past 6 months. This is a matter of deep concern to the President's Science Advisory Committee.

Mr. Fogarty. I personally wouldn't want to see it connected with the National Science Foundation.

COMPETITION BETWEEN NIH AND UNIVERSITIES FOR TOP SCIENTISTS

Mr. Laird. Mr. Chairman, these questions that were raised about difficulties in retaining personnel because of salary scales also raise some interesting side questions.

It looks to me like this problem evolves because of the competition we are creating with Federal funds.

I want to see these scientists and these researchers receive their just reward. I don't think that they always do receive their just reward. But, it seems to me that this competition will know no end. I want to know how we can stop the Federal Government from financing both sides of this competition. It looks to me like that should be given some thought by you and by the Surgeon General.

If it was not for the grants of these Federal funds, you wouldn't be having this competition today. Where does it end?

Dr. Shannon. Let me backtrack a bit and say where it began. I would like to comment on where it ends, or at least where, in my best judgment, it will end. In the first place, when our funds became more generally available, they were available in small amounts as straightforward grants-in-aid; they were not determining factors in influencing the substance of the research that was done, but were rather helpful aids in getting the job done.

As you know, sir, particularly in the past 5 years we have now moved into the position of both stimulating and supporting a broad segment of research that is important to our Nation.

Going back to the initial situation, salaries were so poor immediately after the war that it was scarcely possible for any but a very few to obtain a livelihood in a research career within the medical sciences. So I think that the upward movement of academic salaries, with the aid of our programs, has been a wholly healthy thing.

I would say that the academic salaries themselves are probably set by a combination of forces that are identifiable: (1) Industrial salaries; (2) the availability of career support; and (3) the resources available to institutions. And in the resources available to institutions for support of research, roughly 50 percent comes from our programs.

Finally, there is the interplay between medicine as a profession providing service to individuals, and as a group of scientific disciplines aimed at the creation of new knowledge.

I think that the primary force that determines salary levels within our whole sphere is the interplay between the academically oriented physician and the physician in the practice of medicine. I don't believe that our programs have created this problem. I think our programs, up to the present time, have satisfied some dire needs that had to be satisfied if we were to develop a broad research program for the Nation.

In doing this, we have satisfied the need for adequate salaries in universities well before we have satisfied the salary needs of our own scientists employed in our direct operations. This is the framework, in which I think, the salary question should be considered rather than primarily in relation to the impact of our grant program on the salaries of academically oriented people. This is, as you well know, a very complex problem.

It has certain parallels with the situation in, and the activities of, the Defense Department. I think there is no doubt that defense contracts have inflated salaries in the defense industries. The defense industries face a situation where their major customer is the Federal Government; they not only get the funds from the Federal Government to develop products, but the products that are developed and manufactured are then purchased by the Federal Government.

This is a tighter economy, if you will, than is the case of the scientists in fundamental research or in the medical sciences. I think that things one might be able to do within the Federal Establishment in relation to the development of products which it will purchase itself are somewhat different from a salary situation that is determined by a factor quite extraneous to the research process itself.

In the final analysis, then, I think the universities now have developed, within the science groups, equity—I say equity rather than equality—equity in remuneration with their counterparts in the practice of medicine. There is a balance here where a scientist can retain a position in a university without serious disservice to his salary.

But the general salary level in the universities will be determined more by the general level of the economy, than by what happens in the research area. This is the factor that really is the tie-point to the whole system, in my belief. I think our action should be remedial action aimed at the point where the discrepancies now exist, which is within the Federal Establishment, rather than to attempt to restrain the gains that have been made in the university, which I think have been necessary and are sound.

Mr. LAIRD. I still don't think you have answered my question. Have you given any thought to the idea of setting some sort of a goal that you are going to try to reach but not to go beyond. Or are we just going to continue this competition between you and the medical schools indefinitely, and, as I say, financing it on both sides with Federal funds.

Dr. SHANNON. As I said, I don't believe, sir, we can set a goal because I think the salary that is paid to scientists is only a small part of a larger salary problem that is determined by the return to practitioners in medicine for the services they render. This, in turn, is tied to the economy of the country.

I think research more or less floats in relation to this very broad segment of population. I think that our problem is to maintain some equity that will permit science to have its fair share of the graduates of medicine and the graduates of universities. I think that the numbers we deal with are too small in terms of the total professional group involved for us to be a determining factor in what happens to the total picture.

Mr. Kelly says that our policy is that we only pay what the university salary schedule permits. But the university is influenced so tremendously in its research program by our grants that it can divert its funds in support of personnel when obtaining our funds in support of their research activities.

Mr. KELLY. My thought was that we feel it would be an improper interference for us to establish a salary scale or a limit on the universities; but we do limit it in the sense that we permit the support of salary only to the same extent that they pay salaries to their staff engaged in comparable work outside of defense.

Dr. SHANNON. On the other hand, when we establish regular programs—for instance, in this program that I will speak to in a moment which relates to the designation of research professors—there we impose certain restrictions on the salary the individual can obtain and the work that he can accept.

We put an upper salary of $25,000, and have said that this must be total compensation in the same sense that it is total compensation within the Federal Government.

Mr. LAIRD. I will pursue this a little later, but it seems to me this is in itself a round-robin, too. True, you establish this policy that you won't go beyond the university's salary schedule. But the amount of funds that you put into the university budget has a considerable effect upon that salary schedule. So you get right back to the Federal Government.

I don't know the answer to it. But as I have watched this thing grow, it seems to me that we are encouraging this kind of competition; we are going to be encouraging pirating indefinitely unless a serious study is made of this whole problem.

I don't think such a study has ever been made.

Dr. SHANNON. No, sir, you are right; it has not.

POSSIBLE DISADVANTAGES OF SEPARATING NIH FROM PHS

Mr. DENTON. May I ask a question there. If you did divorce the the NIH from Public Health, would the officers retain their commissioned status and the benefits that they have in such status?

Dr. SHANNON. I think were such a move made, there would be a lot of administrative adjustments that would have to be made. This would be one.

Mr. DENTON. I can think where a man would rather retain his commissioned status for a few years, when he is getting ready to retire, than receive larger pay and lose his status.

Dr. SHANNON. I think this is a peripheral point that would have to be cleared up. I might say there are a lot of quirks in Federal pay conditions that are cumbersome. For example, we cannot, under present legislation, employ a retired Army, Navy, or Air Force officer, however desirable it may be, for our program and have him retain any of the benefits of his service in the Armed Forces. We tried to do this quite recently. We felt there must be some way whereby this would be possible. We find that the AEC has legislation which permits them to do this as a specific exclusion.

There are a lot of quirks in personnel systems; the problem that you pose would be one of the problems that would have to be considered if such an arrangement were envisaged.

I would say that these are minor compared to the general question which could only, I think, be realistically considered by taking a very hard look at the total research function within the Federal Government. In other words, I don't think that any benefit that might accrue from the simple separation of NIH would compensate for the losses, both to the Public Health Service and to the NIH, or that they would warrant such a move, unless a look at science across Government indicated that such a decision should be made on much broader principles than those that would obtain solely to our operation.

I might say that I, as director of NIH, am in a very fortunate position because of the organizational setting in which the NIH finds itself. In an independent operation—whether independent in the sense of NSF or independent as a constituent of HEW—much of my time would be expended in doing those things that are now done by Dr. Terry's office.

I can assure you, sir, this would be a substantial amount of the total time. I feel we are in a protected position where, by and large, I and my immediate staff can address ourselves to the needs of the Nation as encompassed in our programs, to the professional characteristics of our programs, to the interplay between our programs and the university world, without worrying about the political overlay that becomes an essential part of the total operation as soon as it is placed in a more politically sensitive position.

I am using "politics" here in the best sense of the word, in the sense that, as the Army must be governed by civilians, so science must be governed in the final analysis by nonscientists. When we compete for dollars within the Federal budget, the decision as to how much comes to us, as to how much goes elsewhere, is in a broad sense a political decision. It is in this sense that I use the word "politics."

So I have certain vested interests, of a personal nature, in retaining the status quo.

Mr. FOGARTY. Dr. Terry, the Public Health Service has been discussed quite a bit. You feel free to get into the discussion any time you want to—not only on this, but anything else that comes up.

Dr. Terry. I don't know that there is anything I can add beyond what Dr. Shannon has said, Mr. Chairman. I think whether you take individuals or whether you take the entire system as one in the field of medicine and try to separate completely questions of research, of teaching and medical care, one gets into artifical situations, because they are very closely interlinked.

Therefore, as I mentioned to you the other day when this question was posed, we have not given any official consideration to such a question as separating the NIH from the Public Health Service; and I have not been aware of any strong arguments which would influence me in that direction at this time, sir.

Mr. Fogarty. I hadn't thought about this ahead of the time I asked it of the Secretary the other day. But the more we talk about it, the more interesting it is to me. We might develop that further as time goes on. Perhaps some real consideration should be given to it. Maybe it would be a good thing, and maybe it would be the worst thing in the world. I don't know.

Proceed with your statement, Dr. Shannon.

NEW EMPHASIS IN THE GRANT PROGRAM

Dr. Shannon. The change in the character of NIH grant programs, to which I have already referred, reflects a necessary and timely adaptation to the changing relationship between the medical research community and NIH. The need for such an adaptation grew out of the rapid rise in the level of support funds. In response to the public's repeatedly demonstrated desire to accelerate man's age-old war against disease, the Congress, on the recommendation of this committee and its counterpart in the Senate, has substantially increased the appropriation for medical research whenever it could be shown that additional funds could be effectively employed to further this work.

As a result of these actions, NIH expenditure on medical research (excluding research training) has grown by more than a third in each of the last 2 years and is now over five times greater than it was only 5 years ago. These figures are, of course, less startling when they are laid beside the increase in our total national expenditure for research and development, especially in defense-related areas.

Medical research expenditure, from all sources, is still only about 5 percent of total research costs. It is, in fact, sobering to bear in mind that for each dollar spent to improve man's defenses against the inevitable onslaught of disease, so many more must be spent to improve his physical defenses against a possible onslaught by his fellow man.

Nevertheless, the money which the Congress now makes available to the medical research community through the NIH represents a substantial proportion of the total income of most of the medical schools, university departments, hospitals, and other institutions whose research work it supports. The grant programs have greatly stimulated the time and effort expended on research, though this is rarely the sole function—and in most cases not the primary function—of the grantee institutions. Because of this stimulation and the consequent involvement in grant-supported research of so many faculty and staff members, these programs are having an impact on the institutions which NIH must take into serious consideration as the field of biomedical research expands.

The National Institutes of Health has, in fact, reached another new stage in its steady evolution. As a result of the diversity of its categorical and disciplinary interests and the inescapable effects of its programing decisions on the activities of the grantee institutions, NIH must now develop its plans not only in relation to the needs of individual investigators but also in relation to their cumulative impact on the institution.

I do not suggest that the highly successful individual research-project system will not, or should not, remain at the heart of our grant programs—I think it must. But we can no longer remain relatively unconcerned—as we could in the past—about the overall needs of the institutions at which the bulk of biomedical research is conducted.

The maintenance of a proper environment for high-quality work requires that the overall activities of the university department, school, or hospital be soundly planned and intelligently administered by those immediately responsible for them. For this reason it is essential that the mechanisms through which research is supported be clearly designed to subserve the objectives not just of NIH but of the institution itself. A broad approach by National Institutes of Health to major program planning is necessary in order to reserve to these institutions control over their own destinies while, at the same time, preserving the high quality which the research-grant program has attained. The future course of the NIH must, I think, be charted in the light of this new aspect of its role.

I do not wish to give the impression that the National Institutes of Health should relinquish or in any way decrease its responsibility for planning the programs with which to carry out its mission, for thorough review and conscientious assessment of the scientific merits of projects submitted for support, or for the meticulous stewardship of the public funds placed at its disposal. But an organization that accounts for 40 percent of the total national expenditure on medical research must decentralize the decisionmaking process to the fullest extent commensurate with sound public administration and the requirements of law.

If the research done by a medical school, a university department, a hospital, or other research organization is regarded as worthy of governmental support, its research administrators are also worthy of the Government's trust.

Four mechanisms have evolved during the past year or two, or are proposed, to accommodate the changing relationship between NIH and the research institutions. These are:

(1) The consolidation of small project grants into larger program-type grants.
(2) The support of research centers.
(3) The instigation of institutional grants.
(4) A program for career-support for established investigators.

CONSOLIDATION OF SMALL PROJECT GRANTS

Over the past few years there has been a rising trend toward research projects defined in broad and general terms and assured of fairly extensive periods of support. Experience has shown that, with the necessary degree of administrative maturity in academic institutions, these larger grants are a highly productive means of supporting medical research.

In line with this spontaneous development, it is intended, during the coming fiscal year, to urge institutions to consider the consolidation of existing research projects into larger projects which have a coherent central purpose relating to a disease entity, a broad scientific area of inquiry, or to a single scientific discipline. Proposals for the consolidation of existing grants will be at the discretion of the grantee institution and will only be considered after discussions with appropriate faculty members. Financial accountability will, of course, be maintained and the proposed consolidated program must be relevent to the mission of the NIH. The programs must have Council approval.

The consolidation of existing research projects will, I think, be an important step in the continuing improvement of the research project system. An incidental, but nonetheless welcome, benefit will be a reduction in the number of individual applications that would otherwise have to be reviewed by scientists serving on study sections.

Mr. Fogarty. Give us one example there of the consolidation of projects.

Dr. Shannon. Yes, sir. Two years ago when this program was first started, the Division of Biology of the California Institute of Technology was receiving numerous relatively small individual grants.

A team of people from our direct operations, together with council members and study section members, spent a number of days at Cal. Tech. and ended up with a broad program grant of nearly half a million dollars which blanketed these projects into a substantial program aimed at a single overall purpose.

This permitted us, then, to look at the total operation at one time. We feel that this placed more responsible control of the program in the hands of the division of biology. We felt that our advisers—who could look at the total scientific accomplishment of the division, the total resources, together with the total support—had a more coherent picture to evaluate.

Mr. Fogarty. Dr. Rhodes, at Sloan-Kettering, was for some years also trying to get this accomplished.

Dr. Shannon. Yes, sir.

Mr. Fogarty. I thought one of the reasons he used was he was required to do too much bookkeeping, and there was too much bookwork in making application for so many small grants.

Dr. Shannon. Well, Mr. Fogarty, our attitude is that bookwork can be paid for and can be obtained from nonscientific sources. Our feeling is that the project system, when it unnecessarily deals with minute detail, tends to occupy a tremendous amount of the time of the scientist who must be concerned with the development of the specific project.

It also compels him to undertake certain specific programs that he probably would not undertake unless he felt he had some moral obligation to follow through on his proposal.

We feel that the activities in a broader segment of science can be looked at with the same degree of care and with as searching an inquiry, but, instead of involving the individual scientist, involve the people who are higher up in the supervisory chain. We feel this not only frees the scientists from the detailed preparation of small project reports, but provides him with a flexibility of approach to his research on a day-to-day basis that is much more productive than a feeling of compulsion to follow through a program that he has outlined to his peers.

EFFECT ON WORK OF ADVISORY COMMITTEES

Mr. FOGARTY. Would this have any effect on the work of the advisory committees and study sections?

Dr. SHANNON. When we first undertook this, Mr. Fogarty, we felt we would save a tremendous amount of review time and of review dollars by doing it this way. It turns out that we are not saving time and we are not saving dollars, but we are spending them in different and more productive ways.

The advisory groups that are looking at these applications in general, are not the productive scientists that normally look at these project programs on a study section level, but rather are those scientists who have developed broad administrative responsibility and are, therefore, more likely to be at the Council level.

All of these large programs now involve extensive site visits, extensive negotiations, as opposed to putting a series of small projects through a well-geared machine; so that, although we process fewer projects, they are in larger chunks and are individually viewed much more carefully.

So I think that, on balance, about the same amount of time and the same amount of dollars are spent in the review process; but I think this is less disruptive of the time of the scientists who are doing the work—the productive scientists at the study section level who heretofore have reviewed this.

Mr. FOGARTY. You don't mean to say that any applications now bypass the study section?

Dr. SHANNON. No. I will put it this way. They will not bypass the study section mechanism; but they will not go to the conventional study section that looks only at biochemistry or only at physiology, but to a regrouping of the more senior people in the study section setup.

Mr. FOGARTY. I didn't know you had that.

Dr. SHANNON. Yes, sir. We have always had the ability to develop within the so-called study section mechanism such special advisory panels as are required to look at special projects.

Mr. FOGARTY. Do you have special advisory boards, too?

Dr. SHANNON. They all must go to the Council, sir. You might consider these special advisory boards, but we call them——

Mr. FOGARTY. Do you have any special councils for grants?

Dr. SHANNON. No, sir.

Mr. FOGARTY. You don't?

Dr. SHANNON. No, sir. We feel that, regardless of the size or complexity of the grant, it is advisable for one council in one area to look at the total program.

Mr. FOGARTY. All right, go right ahead.

SIZE OF AVERAGE GRANT

Dr. SHANNON. To give you some idea on how far that is going, Mr. Fogarty, in 1960 we awarded 94 research grants of more than $100,000 each.

Mr. FOGARTY. The average is going up, though.

Dr. SHANNON. Yes, sir. The average is going up because the cost of the individual project is going up; because the individuals now are more adequately supported to do a total job.

Mr. FOGARTY. Do you recognize this table?

Dr. SHANNON. No, sir. I have another table which is almost identical with it which was prepared within the last day or two; but it tells substantially the same story.

Mr. FOGARTY. Will it be any benefit putting this table in the record?

Dr. SHANNON. I would like to substitute these figures for yours, sir. Your table was prepared January 23, and that dealt with the first half of the year. We now have had a series of additional actions. The average figure for fiscal year year 1960——

Mr. FOGARTY. Yours is a more up-to-date one?

Dr. SHANNON. Yes, sir.

Mr. FOGARTY. All right, we will put that in the record.

(The table referred to follows:)

AMOUNT OF AVERAGE RESEARCH GRANT, 1955–60

Average grant, fiscal years 1955 through 1960

Institute	1955	1956	1957	1958	1959	1960
NIAMD	$9,605	$10,597	$10,650	$11,622	$13,391	$14,748
NINDB	9,823	10,558	13,834	13,814	16,879	19,256
NCI	11,806	12,423	16,129	16,949	18,190	19,169
NIDR	8,796	8,248	9,826	9,680	10,246	12,119
NIAID	9,617	9,830	10,484	11,945	12,634	13,963
DGMS	8,988	10,758	12,239	12,749	14,596	19,117
NIMH	16,330	14,459	15,280	18,519	18,992	19,297
NHI	11,042	11,870	13,197	14,590	15,957	17,416
Total	10,799	11,489	13,078	14,154	15,560	17,787

NOTE.—In 1960 NIH awarded 94 research grants of more than $100,000 each. This includes the 8 grants for noncategorical clinical centers and the large primate center grant but does not include support for BSIE.

SUPPORT OF CLINICAL RESEARCH CENTERS

Dr. SHANNON. Turning to the development of center grants, the first major step in this direction was the initiation, in 1960, of long-term grant support for clinical research centers. The purpose of the program, in accordance with the wishes of the Congress, is to foster the creation of additional research resources for complex clinical investigations in a broad spectrum of diseases and involving a wide range of scientific disciplines and medical specialties. That this new program is meeting a widely felt and important need has already been amply demonstrated by the response of the medical schools.

During 1960, the first year of the program, support was committed to eight of these centers at an annual cost of $3 million. The role of the multicategorical centers may be illustrated by the fact that during the first 6 months of operation of one of these centers, 19 research projects were approved by the advisory scientific committee set up by the parent institution to coordinate the center's research program and that 10 of these projects were almost immediately activated by patient admissions.

It is just local responsibility for programing and such quick responsiveness to local opportunities for clinical research that we must encourage if a massive support program is to be most effective. In the absence of local administrative freedom and initiative, not only will many valuable research opportunities inevitably be lost but the whole program will be attended by unfortunate disruptions to the educational and service functions of the sponsoring institution and its scientific staff.

At the beginning of the current fiscal year 11 additional general clinical centers were approved which, together with the continuation awards to the first 8 centers, virtually exhausted the $8 million appropriated for 1961. Since then the National Advisory Health Council has considered a number of very promising proposals and there is every reason to believe that during the next few years substantial increases in funds for this program will be highly rewarding.

It is my considered judgment that the general clinical centers will prove to be a very valuable and extremely effective addition to our medical research armamentarium. They have three important virtues: They will give a large number of investigators access to a well-equipped clinical research facility by creating more research beds and their attendant laboratories and by making the beds more readily available to investigators who have only short-term or intermittent need for patient facilities. They will permit the "hot pursuit" of new research opportunities that occur as the result of a new lead, a fresh idea, or the unexpected availability of a particular kind of research patient without restriction as to disease category, and they will strengthen the participating institutions by assuring them of a long period of support and by giving them wide latitude in the design of their research programs within the broad perimeters of the center grant.

Indeed, one of the practical advantages of general clinical centers over the formally designated categorical centers is that the multicategorical centers, by subserving a broader segment of the staff of the institution in which they are located, are more readily adaptable to the shifting needs of active research programs. I am confident that this program amply merits the increased appropriation requested for it.

The extension, in the 1961 appropriation, of the clinical research center concept to include categorical-disease oriented facilities seems well designed to serve both the need of grantee institutions for flexible support and the legal responsibility of the categorical institutes to support research in specific disease areas. This is reflected in many of the applications for categorical center grants which describe the proposed center's research objectives in broad terms, project an interdepartmental and multidisciplinary research program and view the center as providing stable support for a long-term research plan, for additional salaried investigators, and for underwriting the expense of complex research procedures.

In fact, many of the conceptual and administrative difficulties to which this new program has given rise have been due to our perhaps overcautious efforts to set up fairly rigid specifications for these categorical research centers. Although none of these grants have yet been made, it already seems clear that the program will best serve the research needs of the grantee institutions, and thus promote the purposes for which it was conceived, if it is as flexibly administered as the intent of the Congress and the responsible management of public funds will allow.

The applications for categorical research centers at hand, and now being reviewed, indicate that the funds available will be fully utilized by the end of the current fiscal year. An increase of $4.5 million in the appropriation for the financing of additional categorical centers during 1962 is therefore a well-justified request.

PRIMATE CENTERS

A third major step toward the creation and support of new research resources of national significance is, of course, the primate centers program. Construction of one such center, in Oregon, is nearly completed. The experience gained in launching this project—which is the first of its kind in the United States—is now being brought to bear on negotiations for the creation of two or three more of these regional resources.

It may also be desirable to construct at least one center large enough to permit comparative studies on various species of primates, and the increasing difficulty of obtaining suitable primates for research suggests that it may at some future time become necessary to establish breeding colonies for certain species in this country.

CATEGORICAL AND NONCATEGORICAL RESEARCH CENTERS

Mr. Fogarty. Just give me one example of a noncategorical research center and one of a categorical center.

What institutes have them this year?

Dr. Shannon. We have categorical center money this year in heart, cancer, mental, and neurology. The noncategorical program is in the Division of General Medical Sciences. These are clinical centers that are not noncategorical in nature in terms of the disease they deal with, but are noncategorical in the source of their funds—they are multicategorical in operation.

Mr. Fogarty. You have got me confused now.

Dr. Shannon. What I am trying to say is, in operation they study heart, they study cancer, they study mental health, psychiatric problems, and the like. As such, you couldn't consider them noncategorical. But take, for example, the Institute at Hopkins or Maryland or Seattle or Tulane or Atlanta. These units are set up to provide on a centralized basis a number of research beds that may in some cases be as few as 10, or in other cases as many as 25, depending upon the need of the Institute at that time.

These are provided for research purposes in precisely the same way that our own facilities in Bethesda are provided for research purposes. The bed area is accompanied by those laboratories that are necessary, in a general fashion, to support the study of the patient without the whole array of particular apparatus or laboratories that are necessary for a specific project.

Patients are admitted to these areas in precisely the same way as they are admitted to our clinical center. They are admitted for study purposes. They are retained there until the study purpose is completed, and then they are discharged either to their homes or to the general wards.

The predominant cases accepted in most of the Institutes at the present time are in the area of cardiovascular disease, cancer, metabolic disease, and infectious disease, because these are the major general medical problems. But an exception it was felt advisable——

Mr. Fogarty. What about mental health?

Dr. Shannon. Well, sir, one cannot explore the totality of mental health in one of these facilities. There are a number of mental health patients contained in the general facilities, but the Mental Health Institute has under study now and actually has funds in this year's budget for the development of the unique facility that would permit as definitive a study of mental illness as was possible in the more general medical area.

Mr. Fogarty. Does Dr. Felix agree with you?

Dr. Shannon. I think so, yes, sir.

Mr. Fogarty. Does he?

Dr. Shannon. Yes, sir; you can ask him when he comes up. This has been recognized by medical institutions since the development of good clinical investigation in this country. You have the facilities for careful psychiatric studies such as at the Psychiatric Institute in Boston, the Neurological Institute in Boston, and in certain of the privately endowed psychiatric institutes.

But to study the whole array of mental problems requires an overlay of certain conditions from the standpoint of the security of the patients and the peculiar types of studies that must be undertaken in terms of the total environment of the patient rather than the biological environment of the patient. I think there are many problems in the field of mental health that just cannot be performed in this type of general facility.

For similar reasons there are many surgical problems that can't be dealt with in this way. In other words, when one considers the long-range development of this type of clinical center, I think one will envisage a central general medical facility. This is where the bulk of our problems is.

Depending upon the institution, there will also be smaller facilities that will be catering primarily to the needs of the young in the pediatric area, to the mentally ill or to neurological studies, without diminishing the need for the central facility.

I think what we are concerned with right now is building up this central core of a sound clinic investigator program without pretending that we are fully satisfying the need by the program.

EXPLANATION OF NEED FOR CLINICAL RESEARCH CENTERS

Mr. Fogarty. Give me one example of this kind of a program. This was not put in by us in the first place; it was put in by the Senate. We didn't have much information on it when we went to conference, and what we have gotten since is a little confusing to me.

Dr. Shannon. The first need that was sought to be satisfied was to provide an area within a hospital setting for the total quantitative study of patients, primarily in a chemical fashion. In other words, to set up what are called metabolic balance facilities.

Many diseases in metabolism or many diseases that affect metabolism can only be studied if one can measure total intake of an individual, total output, and total activity during the period of observation. This involves a whole array of chemical and physiological techniques—very complex and very costly—that require highly specialized facilities.

Without that, it is quite impossible to study certain metabolic disorders. It is quite impossible to make certain studies on the fate of chemical agents that are being developed as therapeutic tools.

Mr. Fogarty. Let's talk about heart and cancer, as an example.

Dr. Shannon. Take the area that is required to prepare the child with congenital heart disease from the standpoint of the definitive diagnosis of the organic defect, the assessment of the physiological state prior to operation and after an operation in order to determine what has in fact been accomplished by the operative procedure. This is necessary to determine whether what was done on an experimental basis warrants extension as a general therapeutic tool. That may be one example.

Or take the complexities observed in heart failure, where one of the primary disturbances is the ability to handle the sodium ion or salt. We need to undertake balance studies to develop medicinal compounds that will permit the unloading of salt from the body, an essential part of the treatment of cardiovascular failure.

Or the type of experimental setup in myocardial infarction that permits the careful detailed study of agents that are aimed at increasing clotting time and therefore are prophylactic agents in the prevention of further infarction.

EXAMPLE OF A CLINICAL RESEARCH CENTER

Mr. Fogarty. I am still a little bit uncertain as to just what kind of clinical research centers you propose to support. I think if you would pick out an institution and tell us how it has worked, what you support, what some of the results have been, and so forth, it would help me to understand what we are being asked to finance.

Dr. Shannon. We would be glad to give you a detailed analysis of that for the few institutions that have been going.

Mr. Fogarty. Pick out any one; I don't care. I just want to know how it works.

Dr. Shannon. I can just tell you in general terms. We will take Hopkins as an example.

Mr. Fogarty. Do they have 10 or 12 or 50 beds?

RENOVATION COSTS

Dr. Shannon. I believe they have 20, sir. They received a grant April 1 of last year. In preparation for the occupancy of this area, there was a certain amount of renovation that had to be undertaken. I believe they occupied the facility last fall, in September.

Mr. Fogarty. Who paid for the renovation?

Dr. SHANNON. This was paid out of the initial year's grant. That is a problem I would like to return to, if I could.

Mr. FOGARTY. I was just wondering if this was a way we could get hospitals renovated.

Dr. SHANNON. No, sir. This is renovation determined to be essential by the committee which recommends the initial grant.

Occupying the facility, then, early this fall, they had 20 beds available for the quantitative study of disease. They established a committee. The details of this—I would suggest that Dr. Hunt, who runs this program——

Mr. FOGARTY. Dr. Hunt, do you understand what I am trying to get at? I would like you to give me an example, in layman's language, of just what these centers are that we are asked to finance, and the benefits that might be derived from them.

Dr. HUNT. The unit at Johns Hopkins has been admitting patients since the early fall.

Mr. FOGARTY. What kind of patients?

Dr. HUNT. These have been mostly various kinds of medical patients; patients who have normally been taken care of on the medical service; patients with heart disease; patients with the metabolic diseases which Dr. Shannon mentioned.

Mr. FOGARTY. I thought up until this year we had just been dealing with heart and cancer.

Dr. HUNT. The general centers which came under our administration, the first program which was started a year ago, were designed for all departments of the university—recognizing, as Dr. Shannon just said, that certain kinds of patients, mental patients, children, can be taken care of only to a limited extent in these general units.

Mr. FOGARTY. I still don't understand why mental patients are excluded. I thought some report was made a few years ago that more general hospitals should have a ward for mental patients.

Dr. HUNT. They are not excluded as such. Certain types of mental patients can be handled.

Mr. FOGARTY. Am I right or wrong on what I just said—that many experts suggest that new general hospitals ought to provide a wing or a floor for mental patients?

Dr. HUNT. Quite so; these units we are talking about have only 15 or 20 beds. Within such a unit it is hard to have a subunit that is designed for the special needs of disturbed mental patients. You could have an adjacent unit set up for just that purpose, and in some instances this will be done. It hasn't so far. But within a 20-bed unit it is possible to take care of children down to only a certain age, or take care of only the undisturbed mental patients.

So for those very special needs, there will have to be other kinds of units developed. But these general units are designed to serve the general needs of the institutions. All departments, or a majority of the departments, medicine, surgery——

Mr. FOGARTY. So in this instance the first year's grant was practically used up in renovating this section of the building to establish these 20 beds?

Dr. HUNT. The first year of the grant in most instances—and there have been 19 grants made so far——

Mr. LAIRD. How about a list of those in the record at this point?

Mr. FOGARTY. Yes.

SPECIAL REPORT ON CLINICAL RESEARCH CENTERS

Dr. SHANNON. There is a special report on these centers that we can submit which gives a list of all the centers that have an active fund up to the present time.

Mr. FOGARTY. We will put that in the record.

(The report referred to follows:)

CLINICAL RESEARCH CENTERS

BACKGROUND

The clinical research center program was established in the fall of 1959 by the National Institutes of Health as the result of recommendations by the Congress in connection with the fiscal year 1960 Labor, Health, Education, and Welfare Appropriations Act. Design of the program, providing special grants to private research institutions, was in accord with congressional emphasis on the needs for additional biomedical research resources to facilitate the more complex types of clinical investigations in a broad spectrum of diseases and health-related sciences. Responsibility for organizing and operating the general aspects of the program was assigned by the Director, National Institutes of Health, to the Division of General Medical Sciences.

In August 1960, in taking action on the fiscal year 1961 Labor, Health, Education, and Welfare appropriations, the Congress extended to six institutes, also, authority for the establishment of centers for clinical research.

Totally, the National Institutes of Health program aims to provide support for a variety of basic and clinical research efforts on a broad number of diseases and fundamental scientific problems. The clinical center programs of the institutes are concerned primarily with a particular type or group of diseases, such as heart disease or cancer, toward which the work of a particular institute is oriented.

GENERAL (NONCATEGORICAL) CLINICAL RESEARCH CENTERS

Behind the original 1959 congressional action in establishing the clinical research centers were the considerations that (1) clinical research has been insufficiently pursued because of a lack of adequate means to provide the careful observation and control needed for research in the complexities of human biology; and (2) that valuable research in animals or chemical laboratories often has not been carried over into logical correlative studies in human patients because of a lack of proper research facilities and conditions. As one of the principal reasons for these deficiencies the Senate's Report No. 425 of June 23, 1959, cited the high costs associated with clinical research.

The general clinical research center program was planned to help meet these needs, with the concept and design adapted from this guidance in the Senate's report: "The committee has sought competent advice * * * and has reached the judgment that * * * a number of such centralized facilities, either within a single university or among a group of universities, to provide highly integrated research opportunities and services to large numbers of investigators and research groups (should be established)."

Thus a general clinical research center is a resource within a medical institution, aimed at enhancing the quality and quantity of clinical investigations. It is a discrete, physical unit or research ward of about 10 to 20 beds in a hospital, but apart from the general care wards, with a stable, well-trained nursing and dietetic staff to provide precise control and observation, and with directly supporting specialized laboratory facilities.

The grant funds pay for the renovation and equipment of the centers, the costs of the care of research patients (including specialized nursing, diet kitchens, and other services), supporting laboratories, and certain staff salaries.

In these general centers, research scientists can carry on investigations in a wide range of diseases and basic scientific problems. The center facilitates integrated and coordinated efforts between scientists representing different fields or levels of interest. As an example of the possible benefits of such cooperative work, the problem of transplanting human tissues and organs illustrates the need for advances in both the basic sciences, such as chemistry and immunology, and in the clinical sciences, such as surgery and internal medicine, before the important advances in transplantation can be achieved. In addition, however, a general center also can support other types of research ranging from pediatrics to aging and from congenital disorders to internal medicine.

Applications from medical schools, research hospitals, and other public or private research institutions for grants under this program therefore must describe a multicategoric approach under which investigators with varied interests and techniques can share the center's facilities. For administration purposes most sponsoring institutions appoint a director and an interdepartmental supervisory committee.

Qualifications for grants are based primarily on the potential research productivity of the sponsoring institution, the quality of the proposed physical facility, and soundness of the administration to be used in directing the center.

APPROPRIATIONS FOR, AND COSTS OF, GENERAL CLINICAL RESEARCH CENTERS

The recommendations contained in the Senate's June 23, 1959, report were implemented originally for the general clinical research center program in fiscal year 1960 by the addition of $500,000 to the appropriations for each of six of the National Institutes: Cancer, Mental Health, Heart, Arthritis and Metabolic Diseases, Allergy and Infectious Diseases, and Neurological Diseases and Blindness. The total of $3 million, under the administration of the Division of General Medical Sciences, was used to cover the first eight of these center awards in May 1960, totaling $2,974,408, recommended by the National Advisory Health Council in its March 1960 meetings.

For fiscal year 1961, the Congress appropriated $5 million directly to the Division of General Medical Sciences and $3 million to the six Institutes, a total of $8 million, for the continuing support of the general clinical research center program.

On the basis of recommendations by the National Advisory Health Council in its June 1960 meetings, applications for 11 new awards were approved, at a cost of $4,509,702. These new awards, plus the continuation awards for the eight grants made in fiscal year 1960, will require the full amount of $8 million appropriated for fiscal year 1961.

At its November 1960 meetings, the National Advisory Health Council approved four additional awards, and it is expected that in the March 1961 meetings of the Council there may be additional approvals.

PRESENT STATUS OF THE GENERAL CLINICAL RESEARCH PROGRAM

Following is a list of the first eight grants, awarded in May 1960, with a brief indication of the status of each center:

New York University Medical Center, first year's grant, $439,997

A temporary eight-bed clinical research center was approved and began operations on November 1, 1960. The permanent unit probably will be ready for the admission of patients in the summer of 1961.

Johns Hopkins University School of Medicine, first year's grant, $379,054

The first patients were admitted to this 21-bed unit on August 10, 1960. Since the middle of September, occupancy of the center has been running between 60 and 85 percent capacity. Some 18 research projects have been initiated in the center.

Washington University, St. Louis, first year's grant, $338,780

The 15-bed unit was opened October 10, 1960. Within a week a census of 60 percent was established. Patient occupancy is being kept at about the 60-percent level until the professional staff gains greater experience in the mechanics of operating a research facility.

University of Washington, Seattle, first year's grant, $321,248

The 12-bed research facility was opened July 1, 1960. The first two patients in this unit were admitted on July 19. A progressive, planned buildup of census has occurred to date representing maximum current work capacity for the number of nurses thus far employed on the unit. Total hospitalization days on the unit for August 1960 were 79; for September, 105. The average daily patient census for August was 2.5; for September, 3.5. Of 19 research projects approved by the Advisory Scientific Committee within the clinical research center facility, 10 already have been activated by patient admissions.

Emory University, first year's grant, $396,179

The renovation necessary for activation of this 10-bed center now has been essentially completed, and the unit began admitting patients at the end of December 1960.

University of Pennsylvania, first year's grant, $420,421

A temporary five-bed unit to be operated for about 6 months has been approved and began operations in early November 1960. Revisions in plans for the permanent unit have been proposed.

University of Michigan, first year's grant, $357,236

Preliminary plans have been completed and submitted for bid estimates. It was anticipated that the contract for renovation work would be awarded during November 1960. After the award of the renovation contract, the university was to proceed with the appointment of a director for the center.

University of Southern California, first year's grant, $321,493

Renovation is being completed. Nine beds are being planned instead of the original 10 in order to fulfill the State requirements for the minimum number of square feet of space per patient. The director of the center anticipated that the patients would be admitted about January 1, 1961.

Following is a list of the 11 additional awards made by the Division of General Medical Sciences in November 1960:

University of Alabama Medical Center, 1st year's grant	$352, 037
Yale University School of Medicine, 1st year's grant	291, 105
University of Maryland School of Medicine, 1st year's grant	601, 868
Harvard Medical School, Peter Bent Brigham Hospital, 1st year's grant	662, 033
Seton Hall College of Medicine and Dentistry, 1st year's grant	395, 083
Cornell University Medical College, 1st year's grant	650, 607
The University of Rochester School of Medicine and Dentistry, 1st year's grant	244, 696
Duke University Medical Center, 1st year's grant	288, 100
University of North Carolina School of Medicine, 1st year's grant	287, 884
The Ohio State University College of Medicine, 1st year's grant	279, 325
Vanderbilt University School of Medicine, 1st year's grant	456, 264

IMPACT

Information from members of the National Advisory Health Council, special consultants, and deans and faculty members of university medical centers, leads to the conclusion that the concept and functioning of the general clinical research centers are meeting, with considerable success, the needs for which the program was established. In terms of purpose and mode of operation it is felt that the program is making, and will continue to make at an increasing rate, substantive contributions to the national requirements for an improvement and intensification of medical research at the clinical level, especially in the basic biomedical and health-related sciences.

CATEGORICAL CLINICAL RESEARCH CENTERS

In addition to funds for general clinical research centers, Congress appropriated $12 million in fiscal year 1961 to four Institutes for establishment of clinical research centers as follows: National Cancer Institute, $5,500,000; National Heart Institute, $5,500,000; National Institute of Mental Health, $500,000; and National Institute of Neurological Diseases and Blindness, $500,000. In contrast to the program for clinical research centers under the Division of General Medical Sciences which is now in its second year, the first Advisory Council reviews of applications for grants for categorical clinical research centers will not be completed until May 1961. Meanwhile, brief outlines of progress can be reported as follows:

NATIONAL CANCER INSTITUTE CLINICAL RESEARCH CENTERS

The National Cancer Institute is processing applications for clinical center research grants to be financed out of the $5.5 million included for this purpose in the Institute's 1961 appropriation. By early February, 15 applications had been received. Applications will be reviewed by the National Advisory Cancer Council at a special meeting, April 29–30 and May 1. They will be considered particularly from the standpoint of an institution's ability to develop and maintain stable, integrated, multidisciplinary research and training programs.

NATIONAL HEART INSTITUTE CARDIOVASCULAR CLINICAL RESEARCH CENTERS

Following the congressional appropriation of funds for a program of this type, the Heart Institute staff has conducted preliminary negotiations with investigators in a number of medical schools and other institutions. A group of applications has been received and is being prepared for initial review by the Division of Research Grants and for final review by the National Advisory Heart Council later this year. These discussions and resulting applications pertain, for the most part, to a planned program of correlated or integrated research within the institution. It would utilize clinical research resources for which funds were also requested in the applications. Expectations are that over 40 requests will be reviewed and evaluated by the council this year.

Many of the interested institutions view this type of support as stabilizing continued research activities, bringing more effectively into use the especially difficult or costly methods and providing additional stable salaried positions for additional investigators.

NATIONAL INSTITUTE OF MENTAL HEALTH CLINICAL RESEARCH CENTERS

The National Institute of Mental Health has received 11 formal applications totaling over $4 million for the first year of operation of proposed clinical research centers. The proposals focus on such problems as psychosomatic illnesses, mental retardation, autistic children, psychopharmacology and the biochemistry of mental illness.

Preliminary evaluation of these applications by a review committee has indicated that the quality of this particular group of requests is not high and that favorable action might be taken at most on three or four proposals. It is doubtful that any of these applications will be recommended for approval in the full amounts requested.

It is believed that the short time that the applicants had to plan their programs and prepare their applications was an important factor in the quality of the present requests. It is expected that the institutions which preferred to delay submitting an application until they have had more time to assess their needs and plan their programs will be submitting requests which will be more realistic and more promising.

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS CLINICAL RESEARCH CENTER GRANT PROGARM

The National Institute of Neurological Diseases and Blindness clinical research center grant program has as its objective the establishment of a research environment on a university, college, or hospital campus which will provide for a long-term, coordinated clinical research attack on major problems of diseases of the brain, nervous system, and special senses. These clinical research centers usually will be established on an interdepartmental or interinstitutional basis; each center will usually be directed toward either a broad range of neurological and sensury problems such as blindness, deafness, movement disorders, or cerebrovascular diseases, or toward specific disease entities such as glaucoma, otosclerosis, epilepsy, or muscular dystrophy. The centers will provide for a multidisciplinary approach on key problems in these important clinical areas.

During fiscal year 1961, this Institute has 14 applications totaling $2,842,243 in competition for the $500,000 available. The Director, NINDB, has asked 17 outstanding scientists and administrators to advise him on an ad hoc basis on additional research needs which this program should meet, on the technical and administrative criteria for the review of applications, and on the merit of the 14 pending applications.

A special meeting of the National Advisory Neurological Diseases and Blindness Council is being planned for May 1961 at which time these 14 applications and the recommendations of the Director's ad hoc consultants will be considered.

CENTER DEVELOPMENTS

It has become clear that there is a very large unsatisfied demand for general noncategorical clinical research centers which provide the basic resources for a more extensive clinical research program of higher quality for the Nation. It has also become clear in the first year of experience with the administration of categorical clinical research centers that certain modifications may be required in future years to make the program most effective. Essentially, these changes will be in the direction of reducing the specific requirements that grantees must meet in order to be eligible for grants. This tendency toward progressive relaxation of specific requirements for grantees is in accord with the way in which other programs have developed at National Institutes of Health. Typically, during the early phases of research and training programs, lack of experience indicates the desirability of rather specific requirements. As administrative experience is accumulated by the NIH and the grantees, it becomes possible to provide funds unless specific conditions while sustaining responsibility for effective use of public funds.

Dr. Hunt. In most cases the amount of renovation required was such as to take a very large proportion of the first year's award. This varied from place to place. It mostly has been required for the development of the so-called supporting laboratories, the laboratories which are normally immediately adjacent to the ward unit, where the detailed clinical and chemical tests are carried out.

These are not research laboratories, but they are in effect more elaborate clinical laboratories than a hospital normally has for its general patients. This has been the most costly part of the renovation.

Mr. Fogarty. What benefits do we get out of such a program?

Dr. Hunt. The results to date have been only that research has been started.

Mr. Fogarty. Maybe I didn't put the question right, then. What are the hopes for such a program?

Dr. Hunt. The hopes are that this program will give a number of institutions—and eventually a large number, we hope—the opportunity to do with patients the same kind of research that is being done at the Clinical Center here at Bethesda.

The translation of findings that have been made in the laboratory into studies on patients, and from that point the development of therapeutic methods——

Mr. Fogarty. That is the point I had in mind. I thought one of the main reasons for these centers was to get existing knowledge more quickly to these hospital centers and applied to patients. Is that what you have just about said?

Dr. Shannon. I think so; yes.

It is existing knowledge on the laboratory level, which then requires further processing by application to patients on a research basis before it can be made generally available for treatment of patients. You have to go through that additional step.

Mr. Fogarty. But wasn't there an attempt to step up this process of getting knowledge that you have gained out and into medical practice all over the country?

Dr. Hunt. This is exactly why we hope that eventually a large number of medical schools and other research institutions will have the opportunity to do this work.

Mr. Fogarty. Can you foresee in the future an extensive subsidization of hospitals under such a program?

Dr. Hunt. This would be completely unrelated to any subsidization of hospitals, Mr. Chairman, because normally with a 20-bed unit in a 600-bed hospital, there is very little effect on the general hospital operation. But, more than that, these units are designed to be restricted entirely to research patients.

The patients taken care of in the hospital as a whole will not participate in this at all.

NONMATCHING GRANTS FOR CENTER SPACE MODIFICATION

Mr. Laird. Are you insisting here upon the philosophy of the Secretary of Health, Education, and Welfare and the Surgeon General that these renovations be done on a matching basis?

Dr. Hunt. The renovation carried out under these grants has not required any matching.

Mr. Laird. That is what I understood. You think this is a pretty good program, doing it at a complete 100-percent funding?

Dr. Hunt. We believe it is an excellent program. We find that in situations where universities do have to undertake new construction before they can participate in this there was some showing down of their ability to participate.

Mr. Laird. Do you limit this to schools of medicine?

Dr. Hunt. No. Any hospital doing research is eligible. It has to be based on hospitals, since this is clinical research.

Dr. Shannon. Mr. Laird, I would like to clarify one point. That is, I don't think that this should be confused with our research facilities construction program. The testimony, I am afraid, might confuse people.

Mr. Laird. I don't see too much difference, as long as you are spending all the money on renovation this year and on a 100-percent basis. It gets away from the whole philosophy that was expressed in the presentation of research construction legislation by the new administration. It just doesn't seem to me that it is in keeping with that philosophy.

Dr. Hunt. This is limited strictly to renovation of space which is already built and occupied. This is completely different from anything that would qualify or be considered new construction.

Mr. Laird. You don't think any good purpose would be served by requiring matching?

Dr. Hunt. In this area we have permitted renovation under research grants for many years. This happens to be a more extensive part of this particular program, but it is in principle the same thing.

Mr. Laird. I realize the philosophy of the Public Health Service and the Secretary of Health, Education, and Welfare is to give 100 percent in training and research grants and renovation, all the way down the line. But when you come to constructing additional facilities—the crying need that faces medical research—you put up this all-inclusive restrictive requirement. I just want to make the point that here is another case where you are going to give 100 percent financing, but you still keep that blank wall up in front of you as far as new facilities are concerned.

Dr. HUNT. Within the law and regulations, we have to do that.

Mr. LAIRD. There is no law that says you can't do it 100 percent for new facilities. It is authorized in the Public Health Service Act. You are not the witness I should be questioning on this. But I just wanted to use this as an example because it is very much in point.

Mr. FOGARTY. You do have a point there. I don't think it is consistent with the matching formula on new construction.

Dr. SHANNON. I gather you will probably want to discuss this later in relation to the research facilities and construction. I would like to comment on it, but I think it would be better if the comments were in context with the appropriation.

Mr. FOGARTY. Whatever Mr. Laird would desire.

Mr. LAIRD. Go ahead. We can discuss that later.

Mr. FOGARTY. You have some problems, though, don't you, in this program? What are some of the problems?

Dr. SHANNON. That is what I was trying to get back to, Mr. Fogarty. We have, since the beginning, permitted the use of the research grant funds for space modification to achieve the specific purposes of the research grant. In most research grants—we will say the average grant comes to $17,000—remodeling, during the initial year, or in any one year, might amount to $1,000 or $1,500 total; not a very substantial amount.

POSITION OF GAO ON NONMATCHING

When the General Accounting Office recently examined our programs, where renovation was a substantial amount of the initial year's funding, they raised the question of our authority to fund such renovation within the research grant. They pointed out that we could do renovation of this type under the Research Facilities Construction Act, and limited to the dollars available in that appropriation.

We argued that this is not the intent of Congress; this has not been the practice in grant programs of this sort; and we felt we were well within our authority and were well within the intent of Congress to use research grant funds as we have in the past for essential renovation.

They have raised such a serious objection to this practice that they will not be satisfied by anything short of a statement of intent by the appropriation committees concerned. Such a statement should indicate that it is the intent of the appropriating bodies that such proportion of our grant funds as are essential for the achievements of end objects of project grants can be made available for renovation.

I would hope that the committee, in its wisdom, in preparing its report, will comment on this situation, because—short of such a comment—I think our ability to use a dollar for renovation is in jeopardy.

Mr. FOGARTY. Weren't you able to convince the General Accounting Office?

Dr. SHANNON. We were not able to convince them that this was, in fact, the intent of Congress, as judged by past historical presentations before appropriations committees—broad discussions of the type we are having now. But they, that is, the GAO, said that they would insist that it be regularized by a statement by the responsible committees in Congress; otherwise they would have to interpose further objections.

The only thing they have been willing to do so far is to say that they won't interpose an objection until after our hearings.

Mr. DENTON. If the hospitals are already there, why does it cost so much to renovate them?

Dr. SHANNON. I would say this is not renovation; this is space modification. If you go into a university hospital and take over a ward that heretofore has held maybe 40 patients—or a series of semiprivate rooms which, in the aggregate, have held 40 patients—you have to do partitioning to provide space for a smaller number in rooms that would hold one, two, or four or five, or, in some cases, one room as opposed to many small rooms.

Mr. LAIRD. In military construction we consider that as construction. I am on the Military Construction Subcommittee and we have always considered space modification as being construction.

Dr. SHANNON. Let me tell you precisely what we have to do; then you can see how we handle the thing. One has to provide dietary arrangements for the development of diets which are weighed and have known measurable quantities of carbohydrates and proteins in the food. One has to provide the equipment and the installation of equipment that permits the measurement not only of what goes into the patient, but what goes out. And one has to provide other types of equipment for those special clinical procedures that involve special studies on urine, on feces, on gastric juice, and the like that are essential for total documentation of what is happening to this patient in any given space of time.

What we are given, really, is an area in a hospital to develop this facility.

Mr. DENTON. I was in favor of this program, but it looks to me like for 20 patients you are spending a lot of money.

Dr. SHANNON. This is an expensive program. This is the reason why it is done as a special program because it is too expensive to justify as an individual project. The advisory group has to decide whether, in the aggregate, the amount of clinical research that is going on in a given area is sufficiently great and will be helped to a sufficient extent to warrant our undertaking the support of one of these units.

Mr. DENTON. It is kind of a pilot program.

Dr. SHANNON. Yes.

Mr. FOGARTY. This is expensive, whether it is called construction or renovation.

Dr. SHANNON. I hope you call it renovation.

Mr. FOGARTY. Is there anything else you want to say on this problem while we are here?

Dr. SHANNON. No, sir.

Mr. FOGARTY. Go ahead with your statement.

ENCOURAGING BASIC, MULTIDISCIPLINARY RESEARCH

Dr. SHANNON. I would like to turn to another expensive area that is somewhat related in that it involves the making of large grants for general purposes. Many of the most promising medical research frontiers lie in such basic fields as physical biology, molecular biology, biochemistry and virology. For example, the prevention, cure or amelioration of many congenital diseases, including some forms of mental retardation, all await a better understanding of such seemingly remote processes as the mechanisms of protein synthesis.

Mr. Fogarty. What do you mean by that?

Dr. Shannon. Many of these congenital diseases are genetic in origin. The way this genetic information is transmitted from mother to child is through a very complex protein called nucleoprotein.

Defects in the formation of the nucleoprotein transmitting a characteristic from mother to child cannot be studied in the complex unit organism, but must be studied in simple systems.

Mr. Fogarty. Do you think that happens in some forms of mental retardation?

Dr. Shannon. I am sure it does, sir, yes. Even more certainly it is characteristic of a whole series of metabolic diseases that have been studied very carefully, where the defect that causes the disease can be characterized as a deficiency, for example, in a specific enzyme, the characteristics of which are determined by the pattern of protein synthesis, which in turn is conditioned by the nucleic acid that the child inherits from the mother.

In other words, there is nuclear protein that really carries what is called genetic information which determines the capabilities of the individual offspring for growth and, in many cases, its susceptibility to disease. As I say, this can only be studied in very simple systems.

Going back to an earlier statement, I said it is this protein that determines virulence or nonvirulence of the polio vaccine, for instance. This is a genetic characteristic in a relatively simple system. It is only through systematic study of these fundamental processes that one gets clues as to what is characterized in the human as disease causation.

Mr. Fogarty. Is that one of the ways you were able to make some progress with this—this one form of mental retardation? Dr. Felix, is that related to this conversation?

Dr. Felix. Yes, sir.

Dr. Shannon. Phenyl pyrovic oligophrenia is the term you are searching for.

Mr. Fogarty. I have given up trying to remember that word. Is that related to what you have just mentioned?

Dr. Shannon. This is a very good example of what precisely I was speaking of.

Mr. Fogarty. All right, go ahead.

Dr. Shannon. In fact, in the present state of the biological sciences, systematic genetic studies of the traditional fruitfly is more likely to find the real key to a host of congenital diseases than empirical experimentation in the clinics in which their human victims are treated.

Medical research is so much more difficult—and often less productive—than research in the physical sciences simply because the biological sciences lack a systematic and coherent body of scientific law such as the physical sciences developed long ago. This is why it was possible to conceive and build an atomic bomb but is not yet possible to predict or prevent a heart attack.

So long as clinical research is circumscribed by the inadequacy of its fundamental conceptual framework, results will too often be dependent on lucky accidents rather than systematic logical attack.

Continuous, generous, and enthusiastic support for the basic sciences underlying medical progress must be a cardinal point in our national policy for medical research.

It is for these reasons that our programs in recent years have seen the evolution of substantial, multidisciplinary, and stable programs established in the fields of biology, genetics, biochemistry, biophysics, and the communication sciences; as well as in such areas as aging, cardiovascular physiology, and the chemistry of growth. These programs are supported in the regular grants program.

Administrative experience over the past year has shown that all types of large, complicated, long-term grants which involve a substantial institutional commitment must be handled in a special way. It is therefore our intent to establish common administration procedures and review for all grants of the kind described above. We do not envisage the creation of an array of stylized research centers organized and operated in accordance with tightly drawn specifications, but a flexible mechanism which will permit productive adaptation to local needs.

CENTRALIZED SERVICES FOR MEDICAL RESEARCH

Mr. Fogarty. What progress are you making in the provision of services on a centralized basis?

Dr. Shannon. I think we have gone into this far enough to begin to satisfy the needs. In certain areas we are satisfying those needs out of our direct operation. In the case of Dr. Masland's studies, which you may wish to inquire about, we are furnishing quite broad immunological studies that will define the presence or absence of uterine viral infection in the newborn. We are also servicing pathology on a fairly broad base.

In certain of the programs in cancer chemotherapy we are providing other such centralized services. It has seemed to us that as these areas of medical research become broader and more complex, we can no longer finance these programs out of our direct operation at the National Institutes of Health. They will have to be serviced in a more decentralized fashion, either within a given institution or within a given region.

We have currently under review programs in biomathematics in instrument development and specialized animal production. It seems likely that the responsibility for providing those services at times be within the framework of a college or a university as a whole; at other times, the central services can be better undertaken on a regional basis.

We feel that as the complexities of our programs expand, this type of service will become more prominent as an essential part of the total program. I might say that we have undertaken the beginning of this without, at the present time, giving the program any special name.

JONES RECOMMENDATIONS

Mr. Fogarty. Dr. Jones had something new to report on this, didn't he?

Dr. Shannon. They suggested the setting up of a series of centers in much the same sense as I have discussed them. They particularly mentioned biomathematical centers and instrument development centers. I think they were motivated by pretty much the same factors that have motivated us in our program development during the last year or two in that they felt that medicine was being held back by the absence of these very costly and very complex resources that in their view could not even be set up on a university basis but must be set up on a regional basis in much the same way that the primate centers are being set up.

In their budget recommendations to the Senate they had a budgeted item for the development of this type of activity. Mr. Seggel tells me this was $14.5 million. They felt that setting this apart as a separate item, rather than having it just blanketed in as a general grant item, would have the added advantage of making people more fully aware of the need.

Mr. Fogarty. What is in the budget this year for these centers?

Dr. Shannon. We don't have an item in the budget.

Mr. Fogarty. You mean to tell me Dr. Jones recommended $14.5 million, and we don't have anything in the budget for it this year?

Dr. Shannon. Insofar as we go forward this year, this is contained in our general budget, sir—general research programs.

Mr. Fogarty. What happened that Dr. Jones didn't convince the Bureau of the Budget that they ought to accept his recommendations; or has he changed his mind?

Dr. Shannon. There are two points I would make there—one in agreement with the Jones report, and one in disagreement. We felt, too, that this was an important area that should be developed. We felt, however, that it should be developed at a slower rate than the Jones report indicated.

Mr. Fogarty. What did you recommend?

Dr. Shannon. We recommended to the Department, and have their concurrence, that during the initial year a program of this sort would probably be effected at a $5 million level.

Mr. Fogarty. So you think you could use $5 million in 1962?

Dr. Shannon. This was our recommendation to the Department. I believe it was a sound one; yes, sir.

Mr. Fogarty. All right, go right ahead.

INSTITUTIONAL GRANTS

Dr. Shannon. The second new mechanism which is focused on the broad research needs of academic institutions was created by the act authorizing the National Institutes of Health to make grants to medical, dental, and osteopathic schools, and schools of public health for the general support of their research programs. This act was passed at the end of the last session—after the NIH appropriation had been considered by this committee and by the Congress.

In testimony in support of the bill, it was envisaged that the institutional grants would be gradually phased into the NIH grant program by allocating to them 5 percent of the research-project appropriation during the first year and increasing this, by equal increments, to 15 percent in the third year. It has been proposed that the program should be initiated in 1961. The appropriate sum has therefore been set aside in the budget apportionment.

Mr. FOGARTY. This is March 1961 now, and this bill won't get through until May or June and perhaps later. So what are you going to do with that money?

Dr. SHANNON. Actually this is a program that should be forward financed because, in order for schools to make use of funds of this sort that are in total support of their general research activity, we are convinced that it is better if the funds could be anticipated for their use.

So if we could have these funds made available in the 1961 cycle, these funds would be made available for use next year with the institutions being informed now and with payment in June.

BACKLOG OF APPROVED GRANT APPLICATIONS

Mr. FOGARTY. How many approved applications have you on hand that you won't be able to fund, and what is the amount?

Mr. KELLY. The estimate is $18 million. I indicated the other day that this is on the basis of our apportioned funds. We have, I think it is, $6,782,000 for reserve. We are seeking now the release of about $5 million, which would be the reserve funds available in institutes where there is a backlog of projects. So it would be about $13 million that we would currently anticipate.

BUDGET FOR INSTITUTIONAL GRANT PROGRAM

Mr. FOGARTY. How much has been set aside for this program?

Dr. SHANNON. Approximately $12 million, sir.

Mr. FOGARTY. If you were allowed to go through with what you suggest, we wouldn't be able to finance the approved projects.

Dr. SHANNON. This is correct, sir.

I would point out that, in considering the advisability of whether or not these funds should be made available for 1961, we quite appreciate there are factors for and against. We would hold that the most important thing is to establish the program and to get it in operation, rather than to decide whether it begins this year or next year.

We would propose, if authorization for the use of these funds this year is not obtained, to establish the program in 1962, providing this is approved by the House and the Senate, and make the effective date of starting, perhaps, October 1 so that renewal each year would be October 1—thereby giving the institutions approximately 3 months for preplanning since they would know in June or July whether they could expect the funds.

I think that this would substantially accomplish the things that we were trying to accomplish by having a starting date of July 1, using funds of the prior fiscal year.

So, as I say, I think this is one of the most important programs, if not the most important program, contained within this budget. I think it strikes at the heart of the deficiency of our present program, namely, the preservation of institutional stability.

I think the important thing is to start the program rather than to determine whether we start it this year or next year. I feel very strongly about this.

Mr. FOGARTY. Some people seem to think this is one of the easiest ways to get more money. What is your answer to that?

Dr. SHANNON. My answer to that, sir, is that over the long run, if undertaking this program meant that year after year we would have to turn down substantial numbers of research projects, I think it is so important for the stability of the total program that we still should undertake it.

Mr. FOGARTY. Even though you may turn down $25 or $50 million of research grant applications next year if it were approved?

Dr. SHANNON. Yes, sir. I think we have got to the point now where, unless we introduce stabilizing influences in the institution, we shall have a total structure that is shaky.

Mr. FOGARTY. All right, go ahead.

CAREER SUPPORT FOR ESTABLISHED INVESTIGATORS

Dr. SHANNON. The program for the long-term support of career research professorships, recently announced, was similarly designed to increase the research capacity of the medical schools without restricting support to specific, discrete research projects. To a considerable degree, the sound development of research programs is limited by the lack of secure positions for competent investigators who wish to dedicate their careers to research. An urgent need to be met, therefore, is to provide means for enlarging the number of stable career opportunities within the tenure systems of universities and professional schools for research-oriented individuals. It is toward the solution of this urgent problem that the concept of the career research professorship is directed.

However, a review of the first group of nominations for these professorships, and limited consultations with medical school administrators and other advisers, indicates that the program, as now set up, may not be the most effective way to achieve the desired result.

One of the difficulties is that the emphasis on excellence in the present guidelines of the program implies that the award of one of these professorships constitutes formal recognition by the NIH of the professional distinction of the recipient. This interpretation is not only undesirable in itself, but it tends to limit the nominations to senior faculty who already hold tenure positions. Moreover, the universities and other schools quite rightly insist that, as a minimum, it should be their prerogative to determine the title and institutional status of those given awards. They have also raised questions concerning the advisability of Federal selection of individuals to whom the institution must make a career commitment.

We believe there to be some validity to these considerations.

Therefore, though the problem is clear and the need is urgent, we must admit to considerable uncertainty concerning the best mechanisms to be utilized. We have not had sufficient time to explore and discuss all approaches to this problem. Nor have the schools had sufficient time to assess the impact of this program and the role it is to play, or to formulate, in any definitive form, their own views of mechanisms and policies.

Thus, the development of mechanisms of this program must be considered at this point to be an experimental nature. Our experience during this and the forthcoming year will enable us to evolve firm mechanisms for the solution of the major problem upon which further action can be based.

I might point out here, too, that many of the difficulties that the schools find in the utilization of these particular appointments will be removed by the operation of the institution research grant. The uncertainty of this, more than any other single factor, led to, I think, our unsuccessful negotiations during the present year.

As has been the case with all new NIH programs, administrative means must be adjusted for the effective attainment of policy objectives. The necessary and administrative changes are under active consideration and will, I am sure, present no insoluble difficulties.

POSSIBLE AWARD PROGRAM

We are also considering the possible utility—and desirability—of instituting an award which would be purposely designed to constitute national recognition of our most distinguished medical research professors. Such an award would be similar in principle to the Enrico Fermi, or the E. O. Lawrence Memorial Awards given by the Atomic Energy Commission under authority granted by the Congress. This suggestion requires further study. If it merits your consideration, a formal proposal will be laid before you next year.

Mr. Fogarty. Do we have any authority for making awards?

Dr. Shannon. Mr. Chairman, I frankly don't know. I mention this because this came out—the possibility of this type of award—of our discussions with the schools. They pointed out that in the present guidelines, a research professorship meant this type of award to some people and to others it meant something quite different. But, regardless of what it meant, it caused sufficient discussion, among those academically oriented, to lead to the suggestion that there should be within the health field—or within the medical research field—with this country a means for recognizing our distinguished scientists on a national basis.

Mr. Fogarty. It sounds like a good idea to me. I don't know whether you now have legal authority or not to do it.

Dr. Shannon. We have looked into the AEC awards and find that authority to make these awards is contained in the basic act that set up the Atomic Energy Commission. They have two series of awards. One is the Enrico Fermi Award; the other, the E. O. Lawrence Memorial Award. I think we would be inclined toward the latter rather than the Fermi Award.

The Fermi Award is an extraordinary award; it is given infrequently. Fermi was the first recipient. Glenn Seaborg, who incidentally is the present Chairman of the AEC, and John von Neumann are others.

The E. O. Lawrence award—which was in honor of the contributions he made; he was head of the radiation laboratory at the University of California, one of our distinguished nuclear scientists; he died about 4 or 5 years ago——

Mr. Fogarty. Are these awards given while they are living?

Dr. Shannon. They are given to productive scientists during life. In the case of the Lawrence Award they run up to $10,000 apiece.

It seems to me that, were we to establish an award of this general type on a truly national basis and adhere to extraordinarily high standards of selection, it would have the beneficial effect that the Nobel

Prize awards have throughout the entire world. I think they have an effect on the entire educational system. They inspire and encourage youngsters as they see public recognition given to scientists.

This is the thing that is badly lacking in our total system. We don't recognize publicly the competencies we develop.

I just think, not as a personal incentive but as a means of attracting attention to the field and to dignify the entire field, that an award system of this general sort would be very valuable. I am sure that this will have widespread support. We will look into it to find whether we do need other authority or do not.

Mr. Fogarty. You may supply that for the record.

(The following was subsequently supplied:)

While the Public Health Service Act authorizes grants or awards in support of research and research fellowships (42 U.S.C. 242 etc.), the authority is limited to the support of research activities or programs prospectively. It does not, therefore, include honorary awards made solely in recognition of the past accomplishments of the recipient. The Public Health Service has no authority to make such honorary awards to non-governmental persons.

PROPOSED NATIONAL INSTITUTE FOR CHILD HEALTH AND HUMAN DEVELOPMENT

Dr. Shannon. We particularly welcome and strongly support the President's initiative in requesting the Congress to authorize a new National Institute for Child Health and Human Development. It is intended that this Institute should take over from the Division of General Medical Science, the existing Center for Aging Research, and the Child Health Center which is now being established.

Mr. Fogarty. Are you establishing a Child Health Center?

Dr. Shannon. This we could do by administrative devices, sir. It is the development of an administrative focal point for purposes of information, program development, and planning. This requires the approval of the Surgeon General, and this he gave us with the concurrence of the Secretary. So the center, as such, is established.

Mr. Fogarty. I hope you will spell out where the funds are so this committee can take a good look at it.

Dr. Shannon. Yes, sir. As a matter of fact, these come out of funds available to my office, my administrative expenses, and out of Dr. Hunt's office.

Mr. Fogarty. I would like to get it all in one place, because this committee hasn't made up its mind what it is going to do on this yet.

Dr. Shannon. We would like the opportunity at a later time to develop the full specifications of the Institute. I think the center, as such, is not an expensive device. It is the type of organizational entity we create for our own internal planning purposes, and we consider this a part of the normal process of program development, either within the Institute or within my office.

The new Institute, if authorized, will provide a focus for comprehensive and integrated research into the special problem of perinatal and childhood diseases, on the one hand; and of old age, on the other and, in addition, will be the focus of research into the much neglected areas where biomedical sciences merge with the behavioral sciences.

We at NIH have long been conscious of this increasingly important lacuna in our coverage of the broad field of health research and feel that the new Institute will provide a suitable base for exploring this difficult but promising field.

Mr. Fogarty. What is the status of that legislation?

Dr. Shannon. We have cleared the general specifications for Dr. Terry as of yesterday. He has directed his staff to take the drafting of the legislative proposal up with whoever does it in the Department.

Dr. Terry. There is no legislative proposal to date, Mr. Chairman.

1962 BUDGET ESTIMATES

Dr. Shannon. The 1962 appropriation request for NIH operating programs totals $583 million. The new program level represented by this request may be gauged from the base figure of $505 million for 1961. However, if the inclusion of nonrecurring items in the old, as well as the new, figure is regarded as giving better comparability, the appropriate 1961 figure is $536 million.

In addition to the $583 million requested for operating programs in 1962, there are separately identified appropriation requests for the NIH which total $40.3 million, bringing the total to $623.3 million in funds directly related to NIH activities.

Of the separately identified amount, $30 million is for grants for health research facilities construction. This is the final year of the existing authorization and the requested appropriation will bring to $180 million the Federal Government's contribution over a 6-year period, to this sector of the many-sided program to expand the Nation's capacity for medical research.

Although the impact of these grants has been more than doubled by the matching contributions from non-Federal sources, the need for research facilities construction has not yet been fully met. A request for a 3-year extension of the program and an increase in the authorization to $50 million for each of these years has been submitted to the Congress.

Authority will also be sought for Federal construction of facilities that will serve an important national or regional research need and for the operation of such facilities by contract, by transfer to a public or nonprofit institution, or by other suitable means.

The amount requested for direct construction of NIH facilities is $4,630,000. Over half of this sum, $2.8 million, is for essential buildings and utilities at the recently acquired NIH farm in upper Montgomery County. As already mentioned, $700,000 is requested for the planning of additional office space, and $645,000 is needed for the extension of utilities to serve new and proposed buildings. There is also a request for $85,000 for the renovation of facilities for the care and breeding of germ-free animals at Bethesda and $400,000 for the building of staff quarters at the Middle America Research Unit in the Canal Zone.

The remainder of the separately identified amount—$5.7 million—is for the special foreign currencies program which I shall discuss, at the appropriate time, in a separate statement. This will come under a separate appropriation item.

The appropriation request for intramural research shows approximately a 10 percent increase to provide for the expansion of direct research activities in each of the seven Institutes and for the related costs of the central supporting services.

I should like to submit for the record a prepared statement on the programs of the Division of Biologics Standards which is financed from the "General research and services" appropriation.

You will note, Mr. Chairman, that this request also includes $2 million for an increase in the payment of the Federal share of indirect costs on research grants approved on or after January 1, 1962. The justification for this request is forcefully set out in the Jones committee report which described as "a major deterrent to the further expansion of medical research" the drain imposed on the school's own funds by our inability to pay the actual full cost of maintaining the projects we support.

TRAINING GRANTS AND FELLOWSHIPS

There is a net decrease of nearly $14 million in our appropriation request for training grants and fellowships. This results from the inclusion in the 1961 appropriation of a little over $16 million to meet the nonrecurring cost of adjusting the starting dates of training grants so that the schools now have a longer leadtime to make the necessary arrangements. Except for an increase of $2 million for the graduate research training program and an increase of $400,000 for expanding the dental chairside assistant program, we plan to continue the training and fellowship programs at the 1961 levels. I think, Mr. Chairman, that the members of this committee may welcome a brief explanation of the factors which led us to this decision.

Our training programs were designed primarily to meet domestic manpower requirements for the growing research effort. They have succeeded in stimulating the development of many new and improved training situations and have provided personal support for a rapidly increasing number of young scientists through fellowships and through stipends paid by the training institutions from training grants. The program has now become quite large. For the past 4 years, support of training has grown even more rapidly than support of research, and in 1961 it reached the level of $132 million.

Study of the training programs during the past year revealed that they had grown very complex with many special purpose subprograms and unnecessarily disparate rules of eligibility. We have taken steps during the year to reduce the number of levels of fellowships to four and to establish general rules which all institutes follow in the fellowship field. We have thus achieved a more orderly program which retains the ability to meet diverse needs. The program of graduate training grants is still under study, but we have already been impressed by the growing evidence of need for better general support of the graduate educational functions of the institutions which sponsor the training we help finance.

Their needs are for the expansion of physical facilities, and for financial assistance which would lead to a better balance in graduate programs of all kinds, among which specialized research training would find a more stimulating environment. We believe it would be a long range disservice to research training were it to command a disproportionate share of the total educational resources of training institutions.

We have, therefore, enthusiastically supported such measures as full indirect costs of research and the newly authorized program of institutional grants which will give institutions greater ability to support research and research training objectives and to stabilize faculty careers without regard to specific program interests being promoted by our more categorical approaches.

It is our hope also that the Congress will favor the administration's proposals to aid in the production of medical manpower through grants for construction of additional medical school teaching facilities and scholarship assistance to medical students. Our belief is that these steps to strengthen the training institutions and to increase their output have come to be of first importance at this time. These considerations have led the National Institutes of Health to propose no significant increase in the budget for training in 1962. During 1960, training support increased by about $30 million, and in 1961 it is being increased by $40 million more. These are very large adjustments to make in already heavily committed institutions, and we believe that maintaining the newly attained level for another year will give us a much more objective basis for sound recommendations for the future.

Mr. Fogarty. What did the Jones report say on this?

Dr. Shannon. They recommended considerably more.

Mr. Kelly. On a comparability basis they recommended about $13 million more.

Mr. Fogarty. He hasn't changed his mind, has he, since he started working for the Government?

Dr. Shannon. No, sir. Quite frankly, Mr. Fogarty, we went over the Jones report with extraordinary care and had much discussion with the committee during the development of the report. I think, on balance, we are in general agreement with the basic tenets upon which the report was developed and the general conclusions of the group in their advice to the Senate.

But there are contained within the report certain specifics that we have to disagree with, and this is one of them. We feel that at this point of time our recommendation for training support is more logical, in the face of all the circumstances within which the programs are contained, than the Jones report.

I think had we had institutional research grants for 2 or 3 years, had there been general aid programs in the medical schools for a substantial period of time, had there been facilities construction programs that encompassed the training function, then our recommendation would be different.

But in the absence of these things, we feel that our recommendation is sound.

Mr. Fogarty. The Senate bought the Jones program in toto, didn't it, last year?

Dr. Shannon. They did; yes, sir.

Mr. Fogarty. All right, go ahead.

INTERNATIONAL ACTIVITIES

Dr. Shannon. There has, during the past year, been substantial progress in the international activities of the National Institutes of Health. In addition to the further development of programs continued from the previous year, two new programs of particular significance have been launched. These two programs are the international centers for medical research and training and the special foreign currency program.

Obligations for NIH activities outside the United States (exclusive of the foreign currency program) are expected to total $12.8 million in fiscal year 1961 (in contrast to a total of $7.1 million obligated for similar purposes in fiscal year 1960) making this program one of the largest sources of U.S. Federal support for research in foreign countries. Subject to the overall availability of funds, it is expected that research grants made to foreign investigators will continue to increase during 1962.

Mr. Fogarty. I wish you would prepare a statement on the use of Public Law 480 funds; on the establishment of the international centers for research and training, where they are, what they are doing, and what you hope may be accomplished; current commitments to WHO and the Pan American Sanitary Organization; and your relations with the Soviet Union in connection with the exchange program.

(The following was supplied for the record:)

International Activities of the National Institutes of Health, Fiscal Year 1961

GENERAL

A mid-fiscal-year review of the status of the several international activities of the National Institutes of Health indicates substantial progress. Two new programs of particular significance have been launched in addition to the further development of programs continued from the previous year. These two programs are the international centers for medical research and training and the special foreign currency program. Altogether estimated obligations for NIH activities outside the U.S.A. (exclusive of the foreign currency program) are expected to total $12.8 million in fiscal year 1961 in contrast to a total of $7.1 million obligated for the similar purposes in fiscal year 1960. A summary of the current status of certain of the major international activities of the NIH is set forth below by program.

1. Regular research grants and contracts

Research grants and contracts for the support of foreign investigators working on problems relevant to the general and categorical programs of the NIH amounted to $5,008,016 for a total of 303 such awards in fiscal year 1960. Based on applications received thus far and action in the June and November series of Council meetings, it is estimated that comparable figures for foreign research grants and contracts in fiscal year 1961 will be about 425 awards totaling approximately $8,500,000.

At current levels of support, the NIH program constitutes one of the largest U.S. Federal agency programs of support for research in foreign countries. It is expected that the volume of research support for foreign investigators will continue to increase during fiscal year 1962 depending upon the overall availability of funds for research grants.

The basic rationale underlying this growing expenditure for the support of medical research in foreign countries is that there is specific reason to believe that the work supported will significantly contribute to the achievement of the program objectives of the National Institutes of Health. These program objectives, in the first place, relate to progress in understanding and controlling major categorical diseases of national significance and, in the second place, to strengthening and advancing the medical and health sciences and the basic sciences related thereto. In summary the objective of the National Institutes of Health in providing grant support for research carried out by foreign investigators and institutions is to secure the benefits to its program objectives of the superior scientific capability or exceptional research opportunities, which may be presented by such individuals or facilities and their scientific endeavors. Reflecting the above rationale the criteria followed by the National Institutes of

Health in making awards to foreign investigators and institutions, beyond the usual scientific evaluation, are as follows:

1. The research activities proposed must be significantly relevant to the program objectives of the NIH, and
2. The research material is geographically so located that it can best be studied outside the United States, or
3. The research facilities are of such nature or in such location as not to be duplicated with the United States, and
4. The training, competence, or stature of the applicant is such as to provide a high degree of assurance of productive results from the work supported.

2. *Training support*

During fiscal year 1960, a total of $2.1 million was expended by NIH for research training activities on an international basis. Comparable expenditures in fiscal year 1961 are expected to reach $2.3 million. Plans for 1962 based on present budgetary determinations contemplate only a modest increase in these activities.

The NIH international fellowship program is a major element of these overseas training activities. This program, initiated in 1958, provides for supporting the study of outstanding young medical scientists from 34 countries for periods up to 2 years in U.S. universities and research institutions. During fiscal year 1961, it is expected that 90 such awards for a total amount of $700,000 will be made.

Support of U.S. scientists studying abroad under the sponsorship of outstanding research scientists is a program of dominant importance in the array of NIH international activities. In the past 14 years about 650 U.S. scientists have had the benefit of such training and research experience in the laboratories and universities of some 40 countries. During fiscal year 1960, 191 U.S. fellows were supported by NIH training in 28 foreign countries at a cost of $1.2 million. In fiscal year 1961 this program is expected to support a total of 230 U.S. fellows at an estimated level of $1.5 million.

Other NIH overseas training activities include a small number of trainees studying abroad in clinical areas and an estimated $40,000 for training grants to foreign institutions.

3. *Cooperation with WHO and PAHO*

During the past year NIH has worked out agreements with the World Health Organization and the Pan American Health Organization covering the manner in which NIH will cooperate with these organizations in the conduct of research activities sponsored by them. Basically, these agreements provide for preliminary planning of international research programs on a collaborative basis and set forth the terms and conditions under which NIH will support the special research programs of these agencies and the research projects of participating investigators and institutions. Two large research grants for special research projects have been made to the WHO thus far in fiscal year 1961:

(*a*) A grant for the worldwide study of insecticide resistance and for control of insect disease vectors—in the amount of $204,000 for the first year, with support promised for 4 years.

(*b*) A grant for the study of Bilharziasis and research into molluscicides, chemotherapeutics, and diagnostic methods related thereto, in the amount of $78,941 for the first year, with 4 additional years of support promised.

A third grant application providing for the development of global studies relating to the epidemiology of virus diseases is now being reviewed. Applications for support of other comparable large-scale international research programs are expected from WHO. In its March meeting the National Advisory Health Council recommended the approval of a grant of $120,750 to the Pan American Health Organization through the National Institutes of Health for the purpose of planning, developing, and organizing an international health and medical research program for the Americas under the direction of the Pan American Health Organization.

4. *The International Health Research Act of 1960*

On July 12, 1960, the President signed the International Health Research Act of 1960, Public Law 86–610. In general, this act provides for the support in foreign countries of research activities, research training and fellowships, the making of grants and loans of equipment, the support of international health research meetings, and the exchange of research scientists. Although this law does not substantially change the existing authority of the the Public Health Service for the support of activities in foreign countries, it does clarify two matters.

(*a*) It provides an explicit statement of the intent of Congress that PHS programs include the support of health research and research training overseas.

(*b*) It distinguishes clearly the objectives to be sought in overseas health research and training programs.

The Surgeon General and the Secretary of HEW are authorized to support health research and research training in foreign countries for the purpose of advancing the status of the health sciences in the United States. The President is assigned the responsibility of advancing the international status of the health sciences through health research, research planning, and research training in foreign countries.

The President is authorized to delegate any or all of his functions under this act to the Secretary of the HEW, who in turn may delegate these functions for performance to appropriate organizational units within HEW.

A request has been made of the President by the Secretary of HEW for the delegation of these responsibilities to HEW, and it is probable that the National Institutes of Health will be involved in the discharge of these Presidential responsibilities. As of this date, there has been no delegation of the Presidential responsibilities.

In the regular departmental appropriation act of 1961 fiscal year funds a sum of $5 million was designated for the development of activities under the Surgeon General's authorities provided by this act.

Approximately $2.4 million of this amount has been allocated for the development of a series of international centers for medical research and training in accordance with the direction given in the Senate discussion of this particular amount. The remainder of this amount ($2.6 million) will be utilized by the several Institutes and the Division of General Medical Sciences for the support of carefully planned and purposely developed research projects involving foreign investigators and institutions and directed toward research and research training objectives of key significance to these programs. A summary of the status of these activities follows.

(1) *International centers for medical research and training.*—This program envisages the development of a series of international centers for medical research and training based in U.S. universities with an oversea extension in the form of a research laboratory and training facility.

These centers will provide field experience and research opportunities for U.S. postgraduate physicians and scientists and encourage physicians and other health personnel of collaborating non-U.S. institutions to participate in the development of health research and training resources in their national environment.

Each of these centers will consist of (1) a professional, school-based organizational entity which would provide a stable, continuing framework in which programs of medical research, research planning and research training may be conducted in this country, and which is associated with (2) a research and training establishment overseas where these activities may be pursued under environmental, ethnic, and medical conditions which do not prevail in the United States.

By November 23, 1960, the applications of four American universities to sponsor international centers for medical research and training had been approved for payment. The four American universities and their cooperating institutions overseas are as follows:

University of California: University of Malaya, at Singapore, Institute for Medical Research, Kuala Lumpur.

Tulane University: Universidad del Valle, Cali, Colombia.

Johns Hopkins University: All-India Institute of Hygiene, Calcutta School of Tropical Medicine, Calcutta.

University of Maryland: Locations being considered: Medical Colleges at Lahore, Multan, and Rawalpindi, West Pakistan and Dacca, East Pakistan.

Each of the American universities has requested research and training funds ranging from $100,000 to $500,000 per year for each year of a 5-year period. An ad hoc Committee on International Centers for Medical Research and Training reviewed and approved these grant requests, and the National Advisory Allergy and Infectious Diseases Council concurred, recommending to the Surgeon General that these grants be paid.

Of the $5 million appropriated for fiscal year 1961 to support the international centers for medical research and training, $2,269,971 has been transferred from the several categorical appropriations concerned to the National Institute of Allergy and Infectious Diseases which serves as the central point for administering this program. The remainder of the $5 million will be used by the Institutes and DGMS for special foreign research programs in the regular research grants area.

The administrative and staff work concerning these applications is being handled for the time being by the National Institute of Allergy and Infectious Diseases for the five NIH Institutes and the Division of General Medical Sciences which received funds in fiscal year 1961 to support activities implementing the International Health Research Act. The National Advisory Councils of these groups have agreed to make available to the Allergy Council funds appropriated in fiscal year 1961 for this purpose, with the understanding that (1) regular progress and status reports will be made to the other national advisory councils, and (2) that incorporation of the lists of grants awarded in the formal minutes of the other councils will constitute formal endorsement by these councils.

(2) *Special international programing.*—The several Institutes and the Division of General Medical Sciences to which funds under this special international allocation are available are now engaged in planning for the use of the remainder of these funds. Particular objectives meaningful to the program interests of the Institutes and for which there are unusually well suited opportunities for productive work on an international basis will be sought through the projects supported with these funds. A brief summary of the status of this planning by program follows:

(*a*) *The National Institute of Allergy and Infectious Diseases.*—This Institute will utilize funds available for international purposes to support key studies related to the viral, bacterial, parasitic, and fungal infections in warm climates. This group of diseases constitutes a major interest of the Institute. The opportunity for supporting broad studies of these diseases utilizing a variety of scientific approaches and techniques holds the possibility of contributing fundamental knowledge concerning modes of transmission, reservoirs of infection, and relationship of disease incidence and prevalence to climatic conditions and the nutritional status of the people involved. Such basic information may shed light on many difficult, obscure, and unsolved problems in the area of communicable diseases.

(*b*) *The National Institute of Arthritis and Metabolic Diseases.*—This Institute will direct special efforts toward supporting programs for strengthening research and research training in the field of nutrition in Central America in collaboration with the Pan American Health Organization and for a fairly large-scale nutrition research program to be carried out through Columbia University in Beirut, Lebanon.

Further support will be given to research studies ancillary to the work of the Interdepartmental Committee on Nutrition for National Defense in the Armed Forces Institute of Nutrition—one aspect of which will involve research on indigenous cereal protein supplements in Peru.

(*c*) *The National Cancer Institute.*—This Institute plans to explore with U.S. cancer centers, such as Sloan-Kettering, M. D. Anderson, University of California, and others, for a grouping of interests in cancer research with cancer research institutions overseas, to carry out collaborative programs of mutual interest. It is hoped that a wide geographic representation of interest can be developed, by having individual institutions emphasize different area (e.g. M. D. Anderson Institute might be asked to focalize their interest in Latin America). Such grants would make it possible to bring selected foreign research workers who are actively participating in collaborative research to the U.S. institution, but no formal training programs are visualized.

The main impact of these funds would be directed either toward fully established institutions overseas, in which immediate collaborative research of interest to the United States could be undertaken, or toward unusual epidemiological or other situations. An example of the first type of international cancer research would be to bring closer together the immunologists of, say, Roswell Park Institute in the United States and the Karolinska Institute in Sweden. As an example of the second, the investigation by a combined United States-British team of the unusual childhood lymphoma in Uganda, or the collaborative comparative study of gastric and esophageal cancer among the Japanese in Japan, Hawaii, and continental United States.

(*d*) *The National Heart Institute.*—The Heart Institute plans to use the international medical research funds in this fiscal year for the support of research in areas of special importance to the full development of the cardiovascular research field.

It is planned to support research projects particularly in the areas of (*a*) hormones and atherosclerosis, (*b*) lipids and atherosclerosis, (*c*) rheology as it relates to problems of the vascular system, (*d*) epidemiological studies on various ethnic groups and various types of population, (*e*) cerebrovascular investigations. In the development of specific projects in these areas, careful attention will be given to the competence and quality of the foreign institutions and the special opportunities they offer for the research.

Particular attention will be given to the development of cooperative studies of an international character in the heart field.

Opportunities exist and are being explored for the planned exchange of medical research personnel between institutions and laboratories in this country and institutions and laboratories in Latin America and other countries. It is planned to send teams of medical scientists to institutions in Latin America and other countries to demonstrate the more recent techniques in cardiovascular research; and provide limited research funds to foreign scientists after the completion of their research training in this country for projects in their own institutions, utilizing techniques learned here on problems of special programing interest to the Heart Institute.

(*e*) *The National Institute of Mental Health.*—The National Institute of Mental Health proposes the use of these special international funds in two areas of general interest:

(1) Epidemiologic studies of mental health and mental illness in cultures and subcultures other than our own; and

(2) Standardization and comparison on an international basis of psychological nomenclature and classification, diagnostic procedures, etc.

The National Institute of Mental Health has a longstanding interest in the social and cultural factors associated with mental illness. To the extent that any of the variables thought to be related to a disease are limited in range among population groups, the determination of relationships becomes difficult or nearly impossible. For this reason the study of primitive, isolated, and (technologically) underdeveloped sources and cultures represents an opportunity to assess variables in the social and cultural areas that are obscured by the existence of some degree of homogeneity in these factors in Western culture.

Studies of this kind that have been done have been characterized in many cases by inadequate integration of medical behavioral science, and social science approaches, resulting in findings that have some inadequacy. We would propose developing plans to produce adequate collaboration between the various kinds of scientists needed to make studies.

In addition, the National Institute of Mental Health has long been interested in international cooperative studies in the following general areas:

(1) The standardization of procedures and reporting techniques used in statistical reporting of mental illness from mental hospitals and community facilities dealing with the mentally ill and emotionally disturbed.

(2) Standardization of psychiatric nomenclature and the classification of the various mental illnesses.

(3) Comparisons of diagnostic procedures.

(4) Comparison and evaluation of programs for the prevention and control of mental illness.

(5) Comparison and evaluation of programs for the rehabilitation of patients discharged from mental hospitals.

Such studies can be supported by grants to universities and investigators in the United States as well as to those abroad.

(*f*) *The National Institute of Neurological Diseases and Blindness.*—The NINDB envisages two major purposes for its international research program. The first is to utilize resources of trained, highly specialized scientists in disciplines where there are manpower shortages in the United States; the second is to exploit certain unique geographical, social, or environmental situations which provide opportunities for solving specific research problems.

This Institute has relied heavily on the problem commissions of the World Federation of Neurology and, to some extent, on the developing panels of International Brain Research Organization for assistance in defining areas of need, in calling attention to personnel and to laboratories within which programs can be developed, and in formulating certain broad research goals and plans.

The critical disciplinary needs of this Institute are in neurochemistry, neuropathology, and histochemistry, pediatric neurology, epidemiology and biostatistics, and possibly ophthalmology, physiology, and chemistry.

The Institute visualized three possible types of programs for support.

(1) Specific research projects developed independently, or as result of program planning of the problem commissions of the World Federation of Neurology.

(2) Development of a small number of carefully selected research centers within which broad basic research skills will be focused upon critical problems of the categorical diseases.

(3) Formation of cooperative research and training centers through grants made to a laboratory in the United States for research conducted in close collaboration with a laboratory located within a foreign country.

(*g*) *The Division of General Medical Sciences.*—This Institute proposes to use funds available to it under this program for two broad purposes:

(1) To take advantage of unique opportunities of supporting broad epidemiological investigations of chronic disease amongst specific population groups which permit contact of widely dissimilar genetic, constitutional, and environmental characteristics. An example would be the possibility of useful information being derived from the study of the aging populations existing in Israel today. At the present time immigrants from over 20 countries including Yemen, Poland, Hungary, Iraq, Bulgaria, Turkey, Austria, and Germany are being settled in various villages with medical care being provided on a comprehensive basis. Patients are available to participate in these epidemiological investigations, the results of which have great potential for the improvement of medical care generally. Of particular significance, therefore, is the fortuitous gathering together of populations geographically separated for centuries and in which dissimilar genetic and constitutional differences can be isolated and characterized. Already interesting differences of great potential significance have been noted in the incidence of chronic disease between various dissimilar ethnic groups.

(2) Support for a series of studies in the field of human genetics and development utilizing the special facilities of two Japanese universities is intended as a second major area of support under this program. The two universities being considered for this purpose are Kyushu University in Fukuoka and Tokyo University in Tokyo.

At Kyushu University, the particular emphasis of studies would be upon clinical, biochemical, and population genetics. The many offshore islands which have maintained a relatively high degree of isolation provide a rare, natural laboratory for the study of isolation effects upon human populations. Historically, this university has been the intellectual center of the southernmost of the main islands of Japan. Competent younger scientists trained in the United States are on this faculty or are presently in training in this country.

The Tokyo area, with its tremendous population concentration, including several universities and medical schools, offers unusual opportunities for the study of all manner of uncommon developmental disorders. In Tokyo, it would be possible to develop an excellent, rounded program in human genetics using uniquely available materials and embracing all of the currently active areas in this field, such as biochemical, serological, and population studies, biomathematics and clinical human genetics. Using the facilities and faculties thus available on an interuniversity basis, a highly competent staff is already in being to carry through such a program.

5. *Scientific activities overseas* (*special foreign currency program*)

The amount of $3,707,000 was appropriated for fiscal year 1961 to support through use of foreign currencies available under the authority of section 104(k) of Public Law 480, 83d Congress, as amended, scientific activities overseas which give promise of contributing to progress in solution of major health and disease problems. These funds were allocated among eight countries as follows:

Brazil	$160,000
Egypt	287,000
India	1,782,000
Indonesia	88,000
Israel	190,000
Yugoslavia	$400,000
Pakistan	685,000
Poland	115,000
Total	3,707,000

This program is being developed as a direct extension of the intramural research programs of the several Institutes comprising the National Institutes of Health. Research projects developed under this program will be carried out under research agreements with collaborating institutions and investigators in the countries concerned.

The status of the development of this program by country is as follows:

(*a*) *Yugoslavia.*—The Surgeon General, PHS, met with representatives of the Yugoslavian Government in September 1960 as one aspect of a visit with broader purposes and carried out preliminary discussions providing for the detailed negotiations of specific projects. On-site direct discussions between NIH scientists and Yugoslavian scientists are now being conducted to develop a firm agreement.

(*b*) *Poland.*—Preliminary discussions with the Polish Ministry of Health and Ministry of Foreign Affairs were conducted in October 1960, by the Chief, Office of Program Planning of the Office of the Director, NIH. NIH proposals were well received at this time by the Ministry of Health. An NIH scientist participating in this visit held a series of discussions relating to proposed projects with Polish scientists. During February, formal acceptance of the NIH proposed program was received from the Polish Government. Plans are now being made for the visit of a technical team to Poland to carry out detailed "scientist to scientist" negotiations directed toward agreeing upon specific projects for collaboration.

(*c*) *Egypt.*—Preliminary negotiations in Egypt were completed by the Deputy Surgeon General, PHS (representing the Surgeon General) and the Chief, Laboratory of Virology and Rickettsiology, Division of Biologics Standards, NIH (representing the Director, National Institutes of Health) in November 1960. This action has opened the way for scientist to scientist negotiations on individual research projects which will be undertaken in the near future. Discussions have been held with representatives of the Naval Medical Research Unit No. 3 which will participate in these studies to explain proposed research projects and to clarify relationships with the collaborating Egyptian investigators. Detailed project negotiations will be conducted in Egypt in conjunction with a trip now being arranged.

(*d*) *India.*—The Deputy Surgeon General, PHS, and the Chief, Laboratory of Virology and Rickettsiology, Division of Biologics Standards met with officials of the Indian Government in November 1960. Research projects proposed for India by NIH were favorably considered by the Indian Government officials during these meetings. Informal negotiations have taken place between NIH and Indian scientists through correspondence in respect to the details of specific projects. We have unresolved problems at the governmental level in India; however, we have been informed that these problems are currently being worked out and we will be free to negotiate specific projects within the country at an early date.

(*e*) *Pakistan.*—The Deputy Surgeon General, PHS, and the Chief, Laboratory of Virology and Rickettsiology, Division of Biologics Standards met with representatives of the Pakistan Government in December. NIH proposals were favorably received, and detailed negotiations on specific projects were undertaken.

(*f*) *Israel.*—As a result of visits of top NIH staff, overall agreements with the Government of Israel providing for the conduct of specific research projects to be negotiated at the scientist level were concluded early in February. As a consequence of this arrangement a four man technical team visited Israel and has negotiated specific projects. These are being developed into firm research agreements at the present time.

(*g*) *Indonesia.*—Plans are being made for a visit to Indonesia to carry out both government and technical discussions in conjunction with the trip now being planned. Some delay has been experienced in this program due to changes in the assignment of the Indonesian investigators selected for collaboration.

(*h*) *Brazil.*—Formal negotiations of research projects in Brazil have not been undertaken pending renegotiation of the sales agreement to permit specifically the use of funds under section 104(k) of Public Law 480, 83d Congress. According to information received from the Bureau of the Budget, funds are not assignable for medical research under the terms of the present agreement. We have been informed that the negotiations for the change in the sales agreement are in process. In the meantime, there has been informal correspondence between NIH and Brazilian scientists to explore areas of mutual interest as a preliminary to agreeing on specific projects.

6. *NIH-SEATO cholera research program*

The NIH is collaborating with the Southeast Asia Treaty Organization in the development of a cholera research program. Although cholera is fortunately no longer a disease threat in our country, it is a major one in other areas of the world. In May 1959, the SEATO Council initiated a program looking to the eradication of this disease through cooperative research by scientists of all the SEATO nations. The Council allocated $400,000 from the Asian Economic Development Fund for this purpose. The National Institutes of Health was asked to administer the program. In the comparatively short time since initiation of this forward-looking program, a laboratory has been established in Thailand and has functioned for almost a year. Now another more permanent laboratory has been created in Dacca, East Pakistan, which was formerly opened early in December. In conjunction with the opening of this conference, some 50 leaders in cholera research and control from SEATO and other nations gathered in Dacca for a conference on cholera. The Deputy Surgeon General attended this meeting which was jointly sponsored by SEATO and the National Institutes of Health, and for which the government of East Pakistan was host.

7. *United States-U.S.S.R. exchange program—(Thompson-Zhukov agreement)*

The Lacy-Zaroubin agreement under which previous arrangements have been carried out has been superseded by a broader document, the Thompson-Zhukov agreement, signed on November 21, 1959. The provisions of the agreement call on the PHS to assume primary responsibility and implementation of joint meetings, missions, exchanges of publications, and films. Specific proposals are to be negotiated by direct contact between the U.S.S.R. Minister of Health and the Surgeon General, PHS.

1. The National Institutes of Health has been delegated the responsibility to develop plans and to effect three specific provisions of the Thompson-Zhukov agreement. The first (sec. 6:2) calls for a series of reciprocal meetings and cooperation between named research institutions:

   (*a*) Cancer: The National Cancer Institute and the Sloan-Kettering Institute of United States, and the Institute of Experimental and Clinical Oncology of U.S.S.R. agreed to hold joint meetings. The group from the U.S.S.R., consisting of five scientists, visited Sloan-Kettering Institute, September 20–25, 1960, and the National Institutes of Health September 26–28, 1960. It is expected that the United States group will return the visit in May 1961.

   (*b*) Heart: The National Heart Institute held a similar meeting with the Institute of Therapy of the U.S.S.R. The first meeting was held in the United States May 9–21, 1960. The second meeting is scheduled to leave for the Soviet Union in May 1961.

   (*c*) Polio: The Division of Biologics Standards and the research foundation of the Children's Hospital in Cincinnati sponsored a meeting in Moscow, May 12–17, 1960. The second meeting will be held in the United States in 1961.

2. The second specific provision (sec. 6:3) agrees to exchange up to 20 persons, for up to 12 months, for "exchange of experience, or for the conduct of jointly agreed upon research," the latter dependent in part on the development of institutional discussions under section 6:2. Four positions each have been designated to the National Cancer Institute, National Heart Institute, and the Division of Biologics Standards for this purpose. Applications are being received from individual U.S. scientists to spend from 3 to 12 months on specific projects in the Soviet Union. Such applications already greatly exceed the eight positions apparently available under the provision, and plans have been developed between National Institutes of Health and Division of International Health for the methods of selection of applicants. Several names have been presented to

the U.S.S.R. for approval, but no approvals have been obtained to date. The U.S.S.R. has not recommended any fellows for their places. However, it is anticipated that some exchanges will be arranged in the near future.

3. The third specific provision (sec. 6:4) is for an exchange of five missions during 1960–61, of three to six scientists for 3 to 4 weeks. The National Institutes of Health has been given the responsibility to nominate members of the missions and to plan the itinerary and the financing. This responsibility has been further delegated to specific institutes, with coordination in the Office of the Director, National Institutes of Health, as follows:

(*a*) Metabolic diseases, September 20, 1960–October 13, 1960 (National Institute of Arthritis and Metabolic Diseases).

(*b*) Maternal and child care and related research, October 12, 1960–November 11, 1960 (National Institute of Neurological Diseases and Blindness).

(*c*) Infectious diseases and microbiology, for March 1961 (National Institute of Allergy and Infectious Diseases).

(*d*) Medical ecology, for September 1961 (National Institute of Arthritis and Metabolic Diseases).

(*e*) Metabolism and genetics, for October 1961 (National Heart Institute).

(*f*) A U.S.S.R. Mission on Industrial Hygiene visited the United States October 26–November 14, 1960.

The total cost of carrying out the provisions of the United States–U.S.S.R. agreement is estimated at approximately $200,000, spaced over fiscal year 1961 and 1962. This estimate is based on the previous costs of missions, at $2,500 for 5 individuals each of 5 missions; at $2,000 for shorter institutional exchanges, involving 7 members of 3 institutions; and of $5,000 each for 20 individuals for an average estimated period of 4 months. Since the agreement specifies that visits of longer than 6 weeks will be paid for by the host country, at least part of this item will be for fellowships to Soviet scientists chosen to work in U.S. laboratories. The detailed administrative methods for this financing and administrative arrangements have been worked out between the National Institutes of Health and the Division of International Health, Office of the Surgeon General, Public Health Service.

8. *Office of International Research*

The National Institutes of Health has established, as a staff office of the Office of the Director, NIH, the Office of International Research. This office is responsible for coordinating all international activities of the National Institutes of Health. It advises the Director and the Surgeon General on matters relating to the international aspects of medical research and research training and assists the Institutes in the development of international programs. It is specifically responsible for the central administration of all NIH activities utilizing U.S.-owned foreign currencies. The Office constitutes the central point of relationships with the World Health Organization, the Pan American Health Organization, and other international research and scientific organizations. The office is comprised of an Office of the Chief, a foreign grants and awards section, a special foreign currency and program services section, and a program analysis section. The office will also be responsible for establishing and administering NIH offices overseas. A Chief of the Office has been selected and staffing of the component units of the Office is now in progress.

Dr. SHANNON. I think that with that, I could close this section by saying that the purpose of providing grant support for research carried out abroad is to secure, to the benefit of NIH program objectives, the special scientific capabilities of certain foreign investigators or institutions and the exceptional research opportunities often uniquely present in other countries.

Mr. FOGARTY. We will reconvene at 2:30.

AFTERNOON SESSION

Mr. Denton. The committee will come to order.

CLINICAL CENTERS

As I remember, two years ago the Senate included funds for the clinical research centers, and in conference we agreed on a very small operation at the start. And then last year we agreed on the same appropriations as the year before, and the Senate increased it quite a bit, and we agreed on a much larger sum than was in the House bill. Am I right about that?

Dr. Shannon. Yes, sir.

Mr. Denton. Now the one we were supposed to start 2 years ago. Where was that started?

Dr. Shannon. That was started at a level of $3 million under the general title of "General and Metabolic Clinical Facilities."

Mr. Denton. Where was that started?

Dr. Shannon. This was in the Division of General Medical Sciences, and in the first year, eight grants were made. The specifics of that program are covered in a report, and I can furnish you the report.

Mr. Denton. Is that in a report?

Dr. Shannon. That is in a report which we can furnish for the record, Mr. Denton.

The first ones were New York University; Johns Hopkins; Washington University, St. Louis; University of Washington, Seattle; Emory University; the University of Pennsylvania; University of Michigan; and University of Southern California.

Mr. Denton. Now how much did you authorize for each one of those schools?

Dr. Shannon. That was $3 million in the aggregate. The smallest sum was——

Mr. Denton. Oh, I see it. We have it here.

Dr. Shannon. Yes, sir; $321,000. The largest, $401,000.

Mr. Denton. Let us just put this page in the record.

(The information referred to follows:)

Listing of General Clinical Research Centers

Following is a list of the first eight grants, awarded in May 1960, with a brief indication of the status of each center:

New York University Medical Center—first year's grant, $439,997.—A temporary eight-bed clinical research center was approved and began operations on November 1, 1960. The permanent unit probably will be ready for the admission of patients in the summer of 1961.

Johns Hopkins University School of Medicine, first year's grants, $379,054.—The first patients were admitted to this 21-bed unit on August 10, 1960. Since the middle of September, occupancy of the center has been running between 60 and 85 percent capacity. Some 18 research projects have been initiated in the center.

Washington University, St. Louis, first year's grant, $338,780.—The 15-bed unit was opened October 10, 1960. Within a week a census of 60 percent was established. Patient occupancy is being kept at about the 60 percent level until the professional staff gains greater experience in the mechanics of operating a research facility.

University of Washington, Seattle, first year's grant, $321,248.—The 12-bed research facility was opened July 1, 1960. The first two patients in this unit were admitted on July 19. A progressive, planned buildup of census has occurred to date representing maximum current work capacity for the number of nurses thus far employed on the unit. Total hospitalization days on the unit for August 1960 were 79; for September, 105. The average daily patient census for August was 2.5; for September, 3.5. Of 19 research projects approved by the advisory scientific committee within the clinical research center facility, 10 already have been activated by patient admissions.

Emory University, first year's grant, $396,179.—The renovation necessary for activation of this 10-bed center now has been essentially completed, and the unit began admitting patients at the end of December 1960.

University of Pennsylvania, first year's grant, $420,421.—A temporary five-bed unit to be operated for about 6 months has been approved and began operations in early November 1960. Revisions in plans for the permanent unit have been proposed.

University of Michigan, first year's grant, $357,236.—Preliminary plans have been completed and submitted for bid estimates. It was anticipated that the contract for renovation work would be awarded during November 1960. After the award of the renovation contract, the university was to proceed with the appointment of a director for the center.

University of Southern California, first year's grant, $321,493.—Renovation is being completed. Nine beds are being planned instead of the original 10 in order to fulfill the State requirements for the minimum number of square feet of space per patient. The director of the center anticipated that the patients would be admitted about January 1, 1961.

Following is a list of the 11 additional awards made by the Division of General Medical Sciences in November 1960:

	1st year's grant
University of Alabama Medical Center	$352, 037
Yale University School of Medicine	291, 105
University of Maryland School of Medicine	601, 868
Harvard Medical School, Peter Bent Brigham Hospital	662, 033
Seton Hall College of Medicine and Dentistry	395, 083
Cornell University Medical College	650, 607
The University of Rochester School of Medicine and Dentistry	244, 696
Duke University Medical Center	288, 100
University of North Carolina School of Medicine	287, 884
The Ohio State University College of Medicine	279, 325
Vanderbilt University School of Medicine	456, 264

MALARIA RESERVOIR IN MONKEYS

Mr. DENTON. Now, one question I wanted to ask you about is mosquitoes. When I was down in Panama, they were working on yellow fever.

Dr. SHANNON. Yes, sir.

Mr. DENTON. And they said that something besides a mosquito was carrying yellow fever. They were trying to find out what it was. Then they went on to say that monkeys got yellow fever and opossums got yellow fever.

Dr. SHANNON. Yes, sir.

Mr. DENTON. That is, you mean that monkeys and animals like the opossum, get that malaria, too?

Dr. SHANNON. Well, it is conceivable, but it is probably not the case. All mammals have been explored very systematically and, in general, malaria is a disease of primates rather than of lower mammals. And there are a whole host of different parasites that are peculiar to different species, even species of monkeys, if you will, but monkeys, chimpanzees, baboons, gorillas and the like are generally susceptible to this class of disease. But up until very recently, it was thought that there could be crossover between the diseases that were described in the lower primates and the malarias that were described in man.

In attacking the problem, it now has been shown that at least one of these diseases is interchangeable; and this raises the whole question of whether we may not have in our attempts to eradicate malaria, we may not have a whole animal reservoir that must be eradicated, if the disease, in fact, is to be eradicated.

Mr. DENTON. Before, you thought you only had to keep a mosquito away from a man?

Dr. SHANNON. Yes, sir.

Mr. DENTON. Now you have to keep them away from many other things.

Dr. SHANNON. Yes, sir.

CAREER SUPPORT OF ESTABLISHED INVESTIGATORS

Mr. DENTON. When someone endows a chair in the university, is that the same as what you do?

Dr. SHANNON. The main difference is that when you endow a chair, it has to stay in perpetuity in the institution, and the interest from the capital involved is always used as salary for the chair. In our case, what we would do is to provide for the long-term support of individuals for whom we have very good assurance that they are so productive and so excellent that they would compete successfully in the normal grant program for an indefinite period of time.

Mr. DENTON. I think Mr. Kelly answered this question; but the salary that professors receive is determined very largely by the scale of pay at the university?

Dr. SHANNON. Yes, sir.

Mr. DENTON. Not by what you do?

Dr. SHANNON. This is completely true, sir.

Mr. DENTON. And do you have any difficulty that the medical professors are paid more than some other class of professions?

Dr. SHANNON. We do not have any difficulty. But I might say the universities do. A decade ago they felt that their scientists, in general, were grossly underpaid in comparison with other work. But there was not a great deal of difference between the salary of people in science departments and the salary of people in the arts departments.

Now, due to the influx of funds for research and development of both the physical and biological and medical sciences, it has been possible to provide salaries roughly proportional to the need in this category, but there has not been concomitant relief for professors of history, civics, political science, and the like.

So there exists now an even greater inequity between the sciences and the so-called humanities than obtained a few years ago.

Mr. DENTON. Of course, a football coach has always been pretty well paid in most schools. But when I was in law school there was the condition that a law professor was paid a little more than others. I do not know whether this prevails any more.

Dr. SHANNON. I think it does. And I think competition of outside areas is a factor. As I tried to emphasize in connection with the problem of what is a fair salary, there are many factors other than the Federal contribution to the program that determines what a fair salary is. And, in the final analysis, a fair salary is the amount a man can earn competitively in the absence of special favors.

CLINICAL RESEARCH CENTER

Mr. DENTON. Let me just put this in the record on the clinical research centers:

In 1960, the House did not appropriate anything for that purpose. The Senate appropriated $21 million, and the Congress made it $3 million. In 1961, the House appropriated $3 million, the Senate $55 million, and the conference made it $20 million.

GENERAL RESEARCH AND SERVICES, NATIONAL INSTITUTES OF HEALTH

Mr. DENTON. We shall take up now General Research and Services, National Institutes of Health.

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
PUBLIC HEALTH SERVICE			
11 Personnel compensation:			
Permanent positions	1,444	2,023	2,117
Positions other than permanent	29	34	40
Other personnel compensation	69	74	68
Total personnel compensation	1,542	2,131	2,225
12 Personnel benefits	86	138	144
21 Travel and transportation of persons	83	121	168
22 Transportation of things	15	17	21
23 Rent, communications, and utilities	31	37	39
24 Printing and reproduction	16	60	60
25 Other services	97	314	289
Payment to "National Institutes of Health management fund"	990	1,162	1,287
26 Supplies and materials	611	766	844
31 Equipment	297	86	86
41 Grants, subsidies, and contributions	36,555	71,865	82,243
Subtotal	40,323	76,697	87,406
Deduct quarters and subsistence charges	2	2	2
Total, Public Health Service	40,321	76,695	87,404
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
31 Equipment	46		
Total obligations	40,367	76,695	87,404

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	287	362	369
Full-time equivalent of other positions	6	6	6
Average number of all employees	256	330	334
Number of employees at end of year	286	378	378
Average GS grade	5.8	6.5	6.5
Average GS salary	$5,111	$5,861	$5,851

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(*a*) Research	18,263	34,765	45,643
(*b*) Fellowships	5,306	10,100	10,100
(*c*) Training	13,038	27,000	26,500
Total, grants	36,607	71,865	82,243
2. Direct operations:			
(*a*) Biologics standards	2,464	3,095	3,025
(*b*) Review and approval of grants	846	1,440	1,665
(*c*) Administration	196	426	471
Total, direct operations	3,506	4,961	5,161
Total program costs	40,113	76,826	87,404
3. Relation of costs to obligations:			
Costs financed from obligations of other years, net (−)		−131	
Obligations incurred for costs of other years, net	254		
Total obligations	40,367	76,695	87,404
Financing:			
Comparative transfers to other accounts	5,423	7,205	
Unobligated balance lapsing	205		
New obligational authority (appropriation)	45,994	83,900	87,404

Mr. DENTON. Now, Dr. Hunt, if you will go ahead with your statement.

GENERAL STATEMENT

Dr. HUNT. Mr. Chairman, we have submitted a statement for the record. With your permission, I would like to summarize it briefly.

Mr. DENTON. All right.

(The statement follows:)

Mr. Chairman and members of the committee, my statement is on behalf of the Division of General Medical Sciences, which receives its funds under the research and training grants portion of the "General research and services" appropriation. The other Division supported by this appropriation, the Division of Biologics Standards, has been discussed by the Director of the National Institutes of Health in his opening statement.

The Division of General Medical Sciences administers grant programs of the National Institutes of Health for research in the sciences basic to medicine and biology, in public health, and on certain clinical problems not covered by the programs of the Institutes. In addition, the Division administers the grant programs for training investigators in the basic biomedical sciences, provides fellowships for general research training, and directs the NIH Center for Aging Research and the general clinical research center program.

The research and training programs were established, and have grown rapidly, as the result of needs, particularly in certain basic science areas, which could not be adequately met by the disease-oriented, categorical programs of the Institutes.

The medical need for basic knowledge of organic life is growing as an inquiry into specific disease problems, on the one hand, and into specific aspects of the normal order of organic life, on the other. It is tending to disclose fundamental organic relationships which are common to diverse disease categories. Historically, this tendency may be viewed as a natural consequence of the growth and development of the individual fields of scientific knowledge—an inclination for previously separate approaches to converge on common fields of inquiry as gaps are closed in our greater understanding of organic life.

With coordination of progress in the disciplines involved, this tendency to convergence on basic problems of general biomedical concern is bringing about a profound increase in our knowledge of both normal and abnormal life processes and a corresponding increase in our capacity to control them.

In administering its research and training grants for the study of fundamental life processes, a major long-range objective of the Division's program is to aid in the resolution of still incomplete and isolated fields of biomedical knowledge into a more systematized and useful body of knowledge of the whole human organism.

RESEARCH PROGRAM AREAS

On February 8, 1961, the President directed the Secretary of Health, Education, and Welfare to establish a Center for Research in Child Health within the Public Health Service. In accordance with the President's directive, the Secretary and the Surgeon General have created such a center in the Division of General Medical Sciences.

The new center will direct a program aimed at encouraging and stimulating research and research training in the basic biological, behavioral, and clinical sciences related to the problems of childhood and adolescence. It will also strengthen the role of the National Institutes of Health in the multidisciplinary fields related to child growth and development.

The Division is already directing a center with analogous functions, in its Center for Aging Research. In addition, many aspects of the Division's existing programs of research and research training are concerned with matters of significance to child health, particularly in developmental biology, genetics, and the chemistry of life processes.

The research work supported by this Division is classified into six major program areas, each of which involves a number of scientific disciplines.

(1) *The chemistry of life processes.*—The disciplines of this vast field approach life processes according to the elemental molecular and atomic constituents of organic substances; and the elemental chemical reactions of organic function and activity.

All the dramatic physiological events of reproduction, growth, development, aging, disease, and death which are manifested externally in the lifetime of the individual depend on chemically determined mechanisms which initiate or control them. These partially understood mechanisms are on the ultimate frontiers of basic biological and medical investigation. Thus in terms of basic understanding of existing patterns of normal and abnormal life processes, progress in virtually every field of fundamental and health-related research is dependent on expanded inquiry in such chemical fields as biochemistry, physiological chemistry, and toxicology.

In terms of modification and control of existing patterns, the resources of the science of chemistry are almost equally important. The development of chemical methods is essential in every major area of analytical and therapeutic methodology, and many of the most important discoveries in normal and abnormal organic relationships and their useful modification are made by using chemicals to interrupt and thereby disclose those relationships. The field of pharmacology, which concerns the interaction of medically useful chemicals, or drugs, with physiological mechanisms, is essential to this aspect of basic research. Thus, in discussing every other major area of research we are discussing fields in which advances in the chemistry of life processes play an important part.

(2) *Developmental biology.*—This field includes studies of phenomena ranging from the functioning of genes to the processes of cell and tissue specialization in the reproduction, embryologic development, and growth of the individual.

Genetic and immunologic factors common to problems in tissue transplantation as well as embryologic and congenital abnormalities fall in this area, as do many endocrine, nutritional, toxicologic, and behavioral factors in human reproduction and development.

The need for knowledge of factors governing normal and abnormal organic development has been such that the growth of interest in this field has been almost explosive in recent years. If this need can be met by research, it seems likely that the second half of this century will be characterized, from the medical standpoint, by advancement in understanding and control of the intrinsic or internal factors in human development and disease, similar to the advance on extrinsic factors which characterized the first half of the century.

(3) *Clinical fields.*—This area includes research on particular disease problems which are outside the areas of interest of the categorical Institutes; and multidisciplinary clinical projects of general medical interest. Beginning in 1960, grant applications for problems of obvious relevance to more than two of the categorical Institutes of the NIH have been assigned to the Division of General Medical Sciences. Problems in bone and wound healing and repair, principles of treatment in burns and shock, and clinical problems in endocrinology, anatomy, general surgery, anesthesiology, and pediatrics fall in this area.

(4) *Public health, medical care, and nursing.*—Support by the Division in this area provides for research problems in public health and medical care which are not specifically disease-oriented. The program emphasizes: (*a*) methods for providing adequate general medical care; (*b*) techniques of public health practice and their evaluation; (*c*) development of diagnostic and therapeutic measures applicable to large population groups, and field studies to evaluate their effectiveness; (*d*) development of epidemiological and biometric methods applicable to large scale investigations of disease; (*e*) studies of nursing procedures and their evaluation in relation to the patients; and (*f*) the role of the nurse in communicable disease control.

(5) *Methods and tools of science.*—Basic science may be said to be patternseeking; applied science to be patternmaking. In every phase and discipline of biomedical research, the two are inseparable. As the existing patterns of structure and function which constitute normal and diseased life processes are disclosed, parallel needs arise for the rational patterning of new facilities to further explore, analyze, and usefully control them. The need for new forms of research facility of general medical pertinence now ranges from analytical, diagnostic and therapeutic tools and methods for use by individual investigators and practitioners, to large and complex physical environments equipped with computers and electronic and mechanical models of organ systems in which teams of many disciplines may focus in coordinated attack on the more complex biomedical problems. This Division is supporting a substantial amount of research in these areas.

Under this same classification of "Methods and tools of science," the Division also is seeking to improve communications among the biomedical sciences as a whole. The Division is supporting studies of means for making the medical literature more readily available and more useful to scientists; and support is being provided for conferences and meetings of scientists to accelerate the exchange of research findings and problems.

(6) *Clinical research centers.*—The general clinical research center program of the Division of General Medical Sciences is part of a series of programs for the support of clinical research centers being developed by the National Institutes of Health.

Established in the fall of 1959 at the direction of the Senate Committee on Appropriations to help meet national needs for an improvement and intensification of clinical research, the program is intended to provide an adequate means for precise observations and control of research with patients and to extend laboratory research in animals into valid correlative studies in human beings.

The program awards grants to institutions such as medical schools and research hospitals for the establishment of special, discrete, research facilities, centers or units. The grant funds pay for the renovation and equipment of facilities, the costs of the care of research patients (including specialized nursing, diet kitchens, and other services), supporting laboratories and certain staff salaries. The costs of the research carried on in the centers are met by separate project grants or by funds from sources other than the NIH.

The clinical research centers supported by other parts of the National Institutes of Health are concerned primarily with a type or group of diseases, such as heart disease or cancer, toward which the work of a particular Institute is oriented.

In a general clinical research center, various basic and clinical skills are focused on a variety of diseases and on a variety of fundamental scientific problems. As an example, the problem of transplantation of human tissues and organs well illustrates the need for advances in both the basic sciences, such as chemistry and immunology, and in the clinical sciences, such as surgery and internal medicine, before the hoped for breakthrough of successful transplantation can be achieved.

Award of these clinical research center grants is based on an evaluation of the potential research productivity of the applicant institution within the proposed physical facility. Proposals for research projects to be carried on in the centers continue to be reviewed and supported through the regular NIH research grant system.

In these six research areas, during the current fiscal year, the DGMS research grant allocation of $34,765,000 is supporting nearly 1,600 projects, plus certain additional activities.

SPECIFIC RESEARCH GOALS AND ACCOMPLISHMENTS

With regard to current problems and accomplishments in specific areas, it may be of interest to touch on a few highlights at this point to emphasize the interrelatedness of many of our basic and clinical problems. I will begin with some developments in the field of genetics.

Organic form and function are governed from the beginning of life largely by the genes, and many of our more serious diseases either originate in the genes or are subject to genetic influence. Yet the genes have continued to elude accurate definition, and to this day we know very little of what a gene is structurally and how it operates, or fails to operate, in hereditary disease. The value of exposing these genetic operations for possible control in health and disease would be enormous. We need to know how the hereditary information is stored in genetic deoxyribonucleic acid, transmitted to cytoplasmic ribonucleic acid and then put to work by the cell organelles in the synthesis of new protoplasm, new cells, and the agents of differentiation which govern the architecture of organ form and function during individual growth and development.

Some of the chemical and mechanical research problems are now being solved. A clearer definition of the gene is emerging from grant-supported studies in the past year showing direct relationships between particular parts of the genetic apparatus and particular metabolic events. The new findings suggest a genetic architecture in which active elements of the chromosome are lined up in sequence according to the sequences of biochemical events in the metabolic process they control. The findings are preliminary and need to be extended. New biochemical and mechanical tools and approaches are needed for this.

Related studies by other DGMS grantees a few months ago resulted in a promising new method for direct biochemical studies of cell components in the living intact cell. It is hoped that biochemical information on relationships between the genetic apparatus and the sites of biosynthesis it controls will result from current studies in cytochemical methods and resources.

Deoxyribonucleic acid, DNA, the nucleic acid of the genes, is thought to contain in its molecular structures the genetic master plans for the organism, including hereditary diseases. Ribonucleic acid, RNA, in the outer part of the cell, is thought to carry these instructions from the gene to the building sites where they are put into effect in reproduction, growth and development. Many findings concerning the nucleic acids have been made with DGMS support during recent months. Some help explain how nucleic acid molecules may be formed; others pinpoint their sites of origin in the cell. The value of most advances at this basic level of common origins cannot immediately be estimated. One advance by grantees in Israel gives direct evidence that the RNA complex makes and stores the antibodies which form during immunologic reactions. Our greatest present obstacles to successful organ transplantation are immunologic ones, traceable to events at the level of protein synthesis in the cell. Explanations of immunologic responses in terms of genetic and nucleic acid phenomena tend to link major environmental health problems to research problems at the level of the most elemental known units of organic life.

New findings concerning the microsomes of the liver cells also have this effect. The liver microsomes are packages of enzymes with specialized roles in the destruction of substances foreign to the normal economy of the body, such as drugs. One finding indicates that starvation may exaggerate the effects of many drugs by depleting the microsomes of their enzyme proteins. This seems to have implications for research and clinical use of drugs, and perhaps also for understanding individual toxic reactions to environmental poisons. Another study indicates that important industrial poisons such as carbon tetrachloride may produce their characteristic fatty degeneration of the liver by stimulating certain components of the central nervous system which reduce blood flow through the liver and which, at the same time, trigger the release of catechol amines from the adrenal gland. The catechol amines ("adrenalines") normally come into play in stress situations, mobilizing the body's fatty energy reserves. The abnormal mobilization of these lipids in chronic carbon tetrachloride toxicity appears from these studies to lead to their deposition in the liver.

Amines, such as the catechol amines just mentioned, have hormonal roles in the regulation of many neurologically controlled organs and thereby influence emotional, digestive, cardiovascular, and other functions which seem to be prime targets of the major diseases of civilized peoples. A number of clinically important drugs (psychic energizers and tranquilizers) evidently exert effects by inhibiting the enzymes that make and destroy amines in the body. One DGMS-supported advance which may be of interest in this connection affords a way of separating important amines from their enzymes, precursors, and derivatives.

Information of more immediate practical interest is available from studies of the normal physiological roles of unsaturated fatty acids. Some recently announced findings from DGMS-supported studies suggest that the polyunsaturated fatty acids play important metabolic roles in the tissues and cells, probably as active constituents of enzyme systems, and that excesses of dietary saturated fatty acids may lead to progressive depletion of the unsaturated acids and to degenerative changes in the affected tissues. The suggestion has been advanced that the essential fatty acids should be considered as food, not medicine, and that the concept of a balanced intake of saturated and unsaturated fatty acids be incorporated into medical concepts of balanced diet.

Several studies comparing the benefits of whole blood transfusion with those of balanced salt solutions indicate that in many instances where blood is now used, saline has advantages in compensating for shock, chronic anemia, and blood loss during surgery.

Some of our grantees have been concerned with the role, in birth defects, of dietary deficiences during pregnancy. Experimental evidence indicates that a deficiency of vitamin E can influence the production of congenital defects. Other work in both patients and animals shows that the human fetus can actively draw vitamin B-12 and other nutrients from the circulation of the mother and thereby deplete her reserves. The findings reemphasize the importance of medically supervised nutritional care during pregnancy, and point to a need for more knowledge of the transport mechanisms which operate selectively to govern the passage of substances between mother and fetus.

The development of methods and tools of electrocardiography which enable the diagnosis of certain congenital heart defects before birth was also announced by DGMS grantees during 1960. By forewarning of circulatory crisis at birth, this advance may enable lifesaving preparations to be made for cases which can be corrected surgically.

Other potentially lifesaving advances made during the year include a qualitative urinary test for screening suspected victims of lead poisoning. By its speed and simplicity, the test enables early disclosure of patients in whom brain damage is imminent from the swallowing of large amounts of lead, but who do not yet show a clear picture of lead poisoning. The test has special value for children, and has been tried in hundreds of Baltimore children suspected of lead intoxication.

Another DGMS supported study shows that a folic-acid dependent bacterium, *Lactobacilis casei*, can utilize human blood serum as its only source of this vitamin. The discovery makes available a diagnostic procedure useful in distinguishing between megaloblastic anemia caused by deficiency of vitamin B–12 on the one hand and folic acid on the other.

FUND REQUEST

Funds totaling $53,324,000, including $13,500,000 for general clinical research centers, are being requested for research grants during 1962. During fiscal year 1961 funds for research grants totaled $34,765,000, which included $5 million for clinical research centers. The request therefore represents an increase of $18,559,000, of which $8,500,000 is for clinical research centers.

TRAINING GRANTS

It is axiomatic that the Nation's programs of research in the medical and biological sciences are only so strong as our training programs. The quantity and quality of research are directly dependent on the quantity and quality of training, particularly at the graduate levels, with quality being vastly more important than quantity per se. It should be emphasized that training for research clearly implies research experience. As stated in the December report of the President's Science Advisory Committee, with its emphasis on the needs for basic research and graduate training, "It is (the) experience of research that makes a man a scientist."

The character of the general situation embracing research training and research can be described in two similar, interrelated ways: first, the contributions of the Nation's research effort in the fundamental biomedical sciences have continued to grow as more emphasis has been placed on the training of investigators in the basic health-related sciences; but, second, the size of the research programs has remained ahead of the training effort so that critical shortages continue among personnel both to conduct research and to teach.

The shortage continues to have a restraining effect on the research and training efforts of the Federal Government, the private research institutions, private industry involved in health-related programs, the voluntary health groups, and the Nation's medical schools and universities.

There has been considerable progress during the past year in some parts of the total problem. In others, the needs have remained critical or worsened as research advances have exposed new challenges and opportunities demanding new research training efforts. The following four aspects of the total problem have remained crucial, though the exact character of these needs may have changed slightly:

(1) Needs for investigators and teachers in the basic biomedical and health-related sciences far exceed the supply;

(2) Research in the clinical fields is depending even more heavily on advances in the fundamental sciences, and continues to pull personnel out of the basic areas, mainly because of higher salaries;

(3) Many more physician-investigators have put greater demands on university and preclinical science departments for basic science training;

(4) The medical teaching program must be expanded in order for the Nation's supply of physicians to remain adequate for the needs of a greatly expanding population.

The critical significance of meeting all of these needs is forcefully illustrated when we remember it takes between 5 and 10 years to prepare a scientist for a productive career. Training efforts undertaken now are aimed at conditions in 1965 or 1970 when the requirements will be even more severe than now.

Accordingly, the training programs of this Division—including the seven fellowship programs—have been designed (1) to help meet the requirements for trained scientific manpower in the shortage areas represented by the fields basic to medicine and health; and (2) to help meet the growing needs of the Nation's medical schools for academic personnel in both present and future faculties.

More specifically, the DGMS programs have these goals: (1) To aid the research training institutions in developing teachers and scientists; (2) to strengthen the flow of quality students through the graduate schools of the universities; (3) to enlarge the training opportunities for predoctoral and postdoctoral candidates wherever appropriate; and (4) to stimulate and support greater utilization of trained manpower to improve the teaching and training functions of the universities and research institutions.

I will discuss first the training grant program, including the medical student research training grants, and then the fellowship programs.

Research training

This program provides grant funds to public and private nonprofit institutions, such as the medical schools, for the establishment, or improvement, of graduate research training.

Training projects may be supported in any basic biomedical or health-related science where scientific manpower shortages exist. At present the Division is operating regular programs in eleven areas, including: Anatomical sciences, biochemistry, biometry (including biomathematics), biophysical sciences, developmental biology (including cell biology), epidemiology, genetics, microbiology, pathology, pharmacology, and physiology. Each of these programs functions under the guidance of a training committee composed of non-Federal scientists and other experts in the particular field in question.

In addition, upon the recommendations of the National Advisory Health Council and other expert scientific consultants, support at varying levels also is being provided for training in these special fields: Behavioral sciences (other than those related to the program of the National Institute of Mental Health), biomedical engineering, bio-organic and biopolymer chemistry, endocrinology, nutritional sciences, and virology.

During fiscal year 1961, support is being provided in this total of approximately 20 fields for 434 separate research training programs in the medical schools and other private educational institutions across the country.

I should like to discuss the importance of some of these areas:

Biomathematics

This program is designed to place the tools of mathematics and modern computer techniques in the hands of research biologists in a more effective manner. The program includes recognition of the value of theoretical development, in which mathematical representations of biological systems are employed. Programs now receiving support are primarily those in which training efforts have been concentrated upon the application of biostatistical concepts to biology. Additional support is needed for training in theoretical mathematics combined with more profound fundamental training in basic biological concepts.

Biomedical engineering

There is a growing need for improved instrumentation to help observe and record the many variables in the medical and biological sciences. In particular, there is a need for the development of instruments to measure total biological systems above the molecular level. To help bring about a better interrelationship between the engineering sciences and the biological sciences in a stimulation of new concepts and methods, one method would be to develop theoretical and applied training programs. Thus men with broad and deep backgrounds in engineering could become qualified to collaborate with bioscientists at the doctoral level.

Biophysical sciences

This program concerns the dynamic, interdisciplinary area of studies embracing the concepts and methodologies of both biology and physics. Training under this program leads to research in such important fields as radiation biology, the physical properties of macromolecules, theoretical biology and the mathematics of structure-function relationships. The program thus has broad value in a variety of basic and health-related sciences.

Basic endocrinology

It is estimated that a relatively high percentage of all hospital admissions have some basis in metabolic or endocrine disturbance. Because of the manner in which endocrinology reaches into the basic and clinical sciences, there is a genuine need to train scientists in this field, to enable them to take their places in medical and university basic science faculties. Because endocrinology is so tremendously broad, involving nearly all the other preclinical basic sciences, it probably cannot be taught with adequate effectiveness in existing departments of biochemistry and physiology. It requires special attention, and because of its crucial across-the-board importance training efforts in this field must be expanded greatly.

Developmental biology

This field is in need of great stimulation because of the necessary multidisciplinary approach. In general, research in this area is now conducted by individuals or by relatively small groups in a variety of clinical, preclinical, and basic science departments. Bridging the gap between university departments, preclinical departments, and clinical departments (particularly obstetrics and pediatrics) is an immediate objective of an expanded training program in this field. Examples of specific areas where research training is needed of the following: (1) Identification and mode of action of "organizers," the agents responsible for the differentiation of primitive cells into specialized tissues and organs; (2) immunochemistry of embryonic tissues, which differs from that of differentiated tissues; (3) biochemical and electron microscopic studies of the placenta, including investigation of the function of the placenta in controlling gestation; (4) application of biochemical micromethods, now available for analyzing single cells or parts of cells, and of electron microscopy, to embryologic cells.

Bio-organic and biopolymer chemistry

These are terms which broadly define those branches of organic chemistry and physical chemistry, specifically related to biology, lying outside the areas of knowledge customarily term biochemistry. Bio-organic chemistry includes certain branches of natural product chemistry and pharmaceutical chemistry. Biopolymer chemistry is that branch of physical biochemistry concerned directly with the physical chemistry of proteins, polysaccharides and nucleic acids, i.e., the so-called biopolymers. The isolation, identification, and physicochemical characterization of compounds from tissues, the organic synthesis of related materials, and the study of naturally occurring high molecular weight compounds are active areas of reserach in the field of bio-organic and biopolymer chemistry.

Virology

This field is rapidly expanding beyond the classical concepts derived from the study of animal, human, and bacterial viruses, with increasing recognition of the importance of (1) avian hosts as reservoirs for viruses important to the well-being of man, and (2) the relationship of viruses to the etiology of cancer. The shortage of individuals broadly trained in modern multidisciplinary aspects of virology and possessing adequate background knowledge in the fields of tissue morphology and physiology, biochemistry and its subfields of metabolism and enzymology, genetics, and biophysics, is critical. Particularly is this lack of adequately trained personnel felt in medical school faculties. Numerous staff vacancies now exist for which it is impossible to recruit persons with sufficiently broad background and training. Individuals trained in this field will be prepared to become university staff members or members of field and laboratory research teams committed to the exploration of such widely diversified areas as pathogenicity, host susceptibility, epidemiology of viral infections, tissue effects including not only tissue culture but studies of the effect of the viruses upon the total tissue. the permeability of the calls and the synthesis and structure of the cell components.

MEDICAL STUDENT RESEARCH TRAINING GRANTS

This program, formerly called the experimental training grants program, was established in 1957 to carry out experimental efforts aimed toward the improved development of medical scientists and teachers. The Congress annually has provided $500,000 which has gone to 13 medical schools to permit them to adapt in their curricula new features considered necessary to keep pace with increases in medical knowledge. Carefully chosen students have been given special research training to develop their abilities and to stimulate their interest in research and teaching careers.

Last year at this time I indicated to the committee that a study was to be undertaken with a view toward establishing a position as to whether or not this program should be continued beyond fiscal year 1961. The preliminary results of this study indicate rather clearly that the program has been extremely effective in providing research training and experience for medical students. We feel strongly, therefore, that the program should not only be continued but expanded to a total of 20 schools. This would require funds totaling $1,500,000.

FUND REQUEST

For the total research training grant program, including the $1.500,000 for medical student research training grants, funds in the amount of $26,500,000 are being requested for fiscal year 1962, as compared to $27 million for fiscal year 1961. Since there was a nonrecurring expenditure of $1,500,000 in the fiscal year 1961 funds for the forward financing of training grants, the $26,500,000 requested for fiscal year 1962 would represent an increase of $1 million.

RESEARCH FELLOWSHIPS

In contrast to the research training grants, which are made to institutions, the research fellowship awards are made to individuals in order to maintain a measure of flexibility in national programing for the support of research training. The fellowships therefore are complementary to the training awards to institutions. Through several major categories of awards it is possible to provide specific support for newly developing areas and to provide special emphasis at a number of education levels and situations.

The fellowships serve to give students in schools of medicine, dentistry, nursing, and public health, an orientation to, and an appreciation of, basic research; to allow foreign scientists to participate in the research opportunities in this country, and to provide firm, long-range support for young academic staff members with a primary interest in research. As of the end of calendar year 1960 the Division's fellowship programs were assisting more than 2,000 students and scientists in acquiring advanced training.

I will discuss each of the fellowship areas in more detail:

Regular research fellowships

These awards are for the full-time research training of scientists in the fundamental biological and health-related sciences. They are available at the predoctoral and postdoctoral levels and in certain special areas to meet particular requirements. They are available for periods of from 1 year to 3 years in the recognized preclinical sciences and also in other rapidly developing fields, such as embryology and development, medical genetics, biophysical sciences, biomedical engineering, experimental pathology, endocrinology and others.

Senior fellowship grants, special fellowship grants, and career research professorships

The principal purpose of these programs is to establish stable careers for scientists and to help relieve the shortage of researchers and teachers trained in the basic sciences and to aid these scientists in developing their full potential for academic medicine. These awards also help the medical schools, dental schools, schools of public health, graduate schools, and appropriate research institutions in meeting the needs for additional faculty members in the shortage fields such as anatomical and developmental sciences, certain behavioral sciences, biochemistry, biometry, biophysical sciences, epidemiology, experimental pathology, genetics, immunology, microbiology, pharmacology, physiology, virology.

In the case of the career research professorship program, this Division has primary NIH responsibility in the basic biomedical and health-related sciences, including the anatomical and developmental sciences, certain behavioral sciences, biochemistry, biometry, biophysical sciences and others. These fellowships are intended (1) to establish additional full professorial positions in medicine, dentistry, public health, and related areas; (2) to assist in recruiting into these positions persons with the most thorough training and the greatest aptitude and promise for productive careers in research and teaching; and (3) to provide still further incentive for the choice of a career devoted to research and teaching on the part of the young scholars.

Although the program was launched just a few months ago, in the fall of 1960, DGMS already has received a substantial number of applications for these grants.

Research fellowships for foreign nationals

This program supports postdoctoral research fellowships for scientists from other countries at outstanding medical research centers in the United States. The program has proved mutually beneficial in giving the foreign scientists an opportunity to exchange research ideas and techniques with scientists of this Nation.

FUND REQUEST

For the fellowship program, funds in the amount of $10,100,000 are being requested for fiscal year 1962, which would be the same as in the current fiscal year.

CENTER FOR AGING RESEARCH

The Center for Aging Research, a component of DGMS, has the responsibility of serving as the NIH focal point for research in aging. Specifically, the center stimulates and assists the development of new research projects in gerontology at universities, medical centers, and various other research institutions in this country and abroad; maintains liaison among Federal agencies and other organizations supporting programs in aging; fosters the training of additional research personnel; collects and disseminates data related to research in aging; and sponsors conferences, symposia, and seminars on research and training problems in the field of aging.

The center acts as NIH liaison for all programs in this area, thereby providing close cooperation within NIH and between NIH and all Government bureaus and divisions engaged in activities related to aging. In this regard the center acted in an advisory capacity to the White House Conference on Aging and provided technical assistance in planning the conference.

There are no specific funds appropriated to the Center for Aging Research for the conduct or support of research. The costs of research are paid from the appropriations of the seven Institutes of NIH and the Division of General Medical Sciences. However, the center does have the unique opportunity to direct attention to areas of research in aging needing new or additional emphasis. The 15,000 applications for grants received annually at NIH are reviewed by CAR, and those pertaining to aging are categorized, and subsequently incorporated into the center files when acted upon by the Advisory Councils to the various Institutes and Divisions involved in making the grants.

Annually, as a summation of this work, the center publishes a report, "Activities of the NIH in the Field of Gerontology," a review of the extramural as well as intramural projects in the field of aging. The center also publishes the annual "Research Highlights in Aging," which recounts some of the significant findings by NIH grantees in the field of aging.

With the background of information contained in the center's extensive files on research in aging, the professional staff carries out visits to universities, medical schools, and other private research institutions where potentially fruitful research in aging may be undertaken. The staff thus stimulates the development of research in what may be called "gap" areas in aging. Continued efforts are being made to increase study in the three broad areas which are embraced by research in aging: the behavioral and social sciences, the clinical sciences, and the biological sciences. These research activities seek to provide answers to questions relating to the older person's mental health, physical well-being, and and the very basic questions relating to the exact nature of biologic processes and their relationships with disease.

These efforts have had a significant effect in increasing the extramural projects undertaken since the Center for Aging Research was formed. By January 31, 1961, 700 NIH research grant projects were classified within various aspects of aging, as compared with the 274 projects in 1958. During this same period of time, funds supporting this research have grown from $4,570,524 to $16,234,564.

In addition to these expenditures for the extramural programs, approximately another $1 million is spent annually in the intramural programs of the Section on Aging of the National Institute of Mental Health and the Gerontology Branch of the National Heart Institute. All of the other Institutes, as well, are conducting research at varying levels into one aspect or another of the aging process; and it should be noted that since the study of aging often can be closely related to the study of disease, a great part of all the intramural research carried out by the Institutes is significant in the field of aging.

The development of large interdisciplinary programs in four universities for research in aging has produced gratifying benefits. The following brief summaries of the activities of each of these centers show that these programs in aging cover the broad spectrum of subjects which are of key importance to the solution of the problems of aging. They include the aging process as well as the aged individual.

> Duke University, Durham, N.C.: The program involves the entire university, and is heavily oriented in the psychiatric, psychologic, and social sciences. Included are biochemical studies as well as studies on atherosclerosis.
>
> Albert Einstein College of Medicine, New York: This program is being conducted entirely within the medical college. It focuses heavily on the metabolic changes which result from aging, and also includes research in the biochemical, physiological, and pathological alterations. Heart disease is receiving much attention, in addition to those genetic conditions which seem to predispose certain persons to illnesses.
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> Western Reserve University, Cleveland, Ohio: This program involves the entire university and several affiliated hospitals. Principal attention is being given to chronic diseases, particularly in conjunction with studies on rehabilitation. Investigations into the basic biological changes in aging are being carried out also.
>
> University of Miami School of Medicine, Coral Gables, Fla.: This program is entirely basic in its approach to aging. It involves the medical school, the main university, and the marine biology laboratory in interrelated studies in anatomy, physiology, biochemistry, microbiology, botany, and related sciences.

It has been recommended by the CAR and its consultants that more university-wide centers be established, though not necessarily of the magnitude of those now in existence. Smaller centers, called program units, might be established in 40 or 50 institutions throughout the country. The objective of such program units would be to provide mechanisms for stimulating and integrating research interests in aging in atmospheres of common scientific pursuits. In addition to the research which could be carried out by such units, periodic institution-wide seminars of the various aspects of aging would be conducted, and training opportunities and teaching activities would be fostered. The overall plan calls for long-term support for such units.

Following are a few of the findings in aging reported by NIH-supported scientists:

Recent studies show that as the male ages, there is a gradual preponderance of sperm cells containing X chromosomes. As a result, older fathers tend to produce larger numbers of daughters.

It has been determined as a result of long-term studies that changes in the central nervous system lead to slowing of reaction time in the elderly, as well as defects in comprehension, calculation, problem solving, learning, and judgment. While these brain symptoms appear at the average age of 66 years, there is tremendous individual variation. Paranoid reaction in elderly people is not infrequently combined with organic brain defects and is more apt to occur in those who have serious hearing and vision losses. A suicidal attempt is much more likely to be related to a depressive episode that is superimposed upon a lifelong history of hardship.

The relationship of estrogen and coronary heart disease has been a subject of considerable study. Recently it has been determined that women who have had both ovaries removed prior to the natural menopause have a significant increase in atherosclerosis, manifested as coronary heart disease.

Recent studies confirm the fact that animals maintained on diets containing essential nutrients, but limited in caloric content, have an increased lifespan and a tendency to postponement in the development of tumors and kidney disease.

Findings on loss of muscle tissue during aging have been reported. The degree to which aging affects the various tissues of the body is markedly different. One explanation for this observation is the extent of cellular loss from the various tissues with age. It has been proposed that tissues whose cells are capable of reproducing themselves (such as liver) exhibit a smaller cellular loss than those whose cells are not capable of reproduction (such as muscle). Marked loss of muscle tissue in aged rats was demonstrated by gross organ weight as well as chemical changes within the muscle mass. The chemical changes suggested a loss rather than atrophy of the muscle fibers. On the other hand, no significant age changes were observed when liver was examined.

With considerable attention being paid to unemployment, it is interesting to note that researchers in the Institute of Labor and Industrial Relations, University of Michigan and Wayne State University of Detroit, have completed a study on the "Social, Psychological, and Situational Factors in the Morale of Unemployed Industrial Workers." Fifty percent of the persons studied were over 55 years of age. The report on this research stated that the old folk adage "busy hands make for happy hearts," was found to be only partly true. The "happy heart" of the reemployed worker (his morale) does not depend on work alone but on work that is comparable in status to his former job.

During the past year we were fortunate in obtaining a full-time director for the Center for Aging Research. He is Joseph H. Gerber, M.D., most recently medical officer in charge of the Indian Health Area Office, Aberdeen, S. Dak.

Dr. Gerber received the M.D. degree from New York University School of Medicine, New York City, in 1933, and the Dr. P.H. from Yale University School of Medicine, New Haven, Conn., in 1948. He served as assistant director of the Peter Bent Brigham Hospital, Boston, from 1948 to 1949, and as assistant medical director of the Health Insurance Plan of Greater New York from January 1949 to July 1950. He had served in the U.S. Army as flight surgeon in the Mediterranean theater from September 1942 to June 1945.

CONCLUSION

In conclusion, Mr. Chairman, the amended request for the Division of General Medical Sciences for 1962 is a total of $92,291,000 as compared with the adjusted appropriation of $73,758,000 for 1961. The allowance for 1962 will provide for an increase of $18,559,000 in research grants; an increase of $198,000 in review and approval for professional and clerical staff engaged in processing, analyzing, and managing research and training grants; an increase of $241,000 representing this Division's share of costs for review and approval and administrative services furnished centrally; and an increase of $35,000 for overall planning, direction, and coordination of the programs of this Division.

The request for 1962 is distributed among program activities as follows:

Grants:	
Research	$53, 324, 000
Fellowships	10, 100, 000
Training	26, 500, 000
Subtotal, grants	89, 924, 000
Direct operations:	
Review and approval of grants	1, 886, 000
Administration	481, 000
Subtotal, direct operations	2, 367, 000
Total 1962 Division request	92, 291, 000

Dr. Hunt. Mr. Chairman and members of the committee, this statement is on behalf of the Division of General Medical Sciences which receives its funds from the research and training grants portion of the "General research and services, NIH" appropriation.

This Division administers grant programs for research in the sciences basic to medicine and biology, in public health, and on certain clinical problems not covered by the programs of the Institutes. The Division also administers the grant programs for training investigators in the basic biomedical sciences, provides fellowships for general research training, and directs the NIH Center for Aging Research, the new Center for Research in Child Health, and the General Clinical Research Center program.

CENTER FOR RESEARCH IN CHILD HEALTH

On February 8, 1961, the President directed the Secretary of Health, Education, and Welfare to establish a Center for Research in Child Health within the Public Health Service. In accordance with the President's directive, such a center has been established in the Division of General Medical Sciences.

The new center will direct a program aimed at encouraging and stimulating research and research training in the basic biological, behavioral, and clinical sciences related to the problems of childhood and adolescence. It will also strengthen the role of the National Institutes of Health in the multidisciplinary fields related to child growth and development.

The Division is already directing a center with analogous functions, in its Center for Aging Research. In addition, many aspects of the Division's existing programs of research and research training are concerned with matters of significance to child health, particularly in developmental biology, genetics, and the chemistry of life processes.

RESEARCH RESPONSIBILITIES OF THE DIVISION

The research responsibilities of the Division fall into six principal areas. The first two, chemistry of life processes and developmental biology, are concerned with the study of fundamental life processes, including all the dramatic physiological events of reproduction, growth, development, aging, disease, and death. The disciplines of this vast field play a part in our discussions of every other major area of research, and, in recognition of the need for such basic research, about half of the Division's total research funds go into these two categories.

The other four categories are clinical fields; public health, medical care, and nursing; methods and tools of science; and clinical research centers. During the current fiscal year, approximately 1,600 projects are being supported in these areas.

TRAINING PROGRAMS

The training programs of this Division have been designed to help meet requirements for trained scientific manpower in the shortage areas represented by the fields basic to medicine and health and to help meet the growing needs of the Nation's medical schools for academic personnel in both present and future faculties. At present, the Division is operating regular programs in 11 areas: Anatomical sciences; biochemistry; biometry (including biomathematics); biophysical sciences; developmental biology (including cell biology); epidemiology; genetics; microbiology; pathology; pharmacology; and physiology. For greater flexibility in training, research fellowships are awarded to individual scientists at various stages of their training.

CENTER FOR AGING RESEARCH

In the field of aging, the NIH Center for Aging Research acts as the NIH focal point for research in this field. The center stimulates and assists the development of new research projects in gerontology at universities, medical centers, and other institutions in this country and abroad and acts as NIH liaison for all programs in this area. Total support by all the institutes and this Division of research grant projects on the various aspects of aging has increased from 274 projects at a cost of $4,570,524 in 1958 to 700 grant projects at $16,234,564 as of January 31, 1961.

In conclusion, Mr. Chairman, the amended request for the Division of General Medical Sciences for 1962 is a total of $92,291,000 as compared with the adjusted appropriation of $73,758,000 for 1961. The allowance for 1962 will provide for an increase of $18,559,000 in research grants; an increase of $198,000 in review and approval for professional and clerical staff engaged in processing, analyzing, and managing research and training grants; an increase of $241,000 representing this Division's share of costs for review and approval and administrative services furnished centrally; and an increase of $35,000 for overall planning, direction, and coordination of the programs of this Division.

The request for 1962 is distributed among program activities as follows:

Mr. Denton. You may have the table placed in the record at this point.

(The table referred to follows:)

Grants:	
Research	$53, 324, 000
Fellowships	10, 100, 000
Training	26, 500, 000
Subtotal, grants	89, 924, 000
Direct operations:	
Review and approval of grants	1, 886, 000
Administration	481, 000
Subtotal, direct operations	2, 367, 000
Total 1962, amended request	92, 291, 000

Dr. HUNT. Thank you, sir. That is the end of our statement. I will be glad to answer any questions that you may have.

1962 BUDGET REQUESTED

Mr. DENTON. How much did you originally request?

Dr. HUNT. The request to the Public Health Service? Was that your question, sir?

Mr. DENTON. Yes. You have to go through Public Health first.

Dr. HUNT. The preliminary estimate to the Public Health Service for all activities, including $3,050,000 for the Division of Biologics Standards, was $104,032,000.

Mr. DENTON. And how much did HEW cut you?

Dr. HUNT. The submission by the Department to the Bureau of the Budget was a total of $95,767,000.

FUNCTIONS OF THE DIVISION OF GENERAL MEDICAL SCIENCES

Mr. DENTON. Now, your Division has always been a sort of a catch-all; what was not covered in the specific agencies was covered by your Division.

Dr. SHANNON. May I comment on that?

Mr. DENTON. That is not quite right?

Dr. SHANNON. It puts the Division Chief in a bit of an embarrassing position.

This is how the Division originally functioned, as a straight catch-all for those programs that did not fit neatly in one or the other of the categorical programs.

But in the summer of 1958, as a matter of policy, we assigned to this Division certain broad programs in both research and research training that, while they could fit and had been carried theretofore under the categorical programs, we felt could be better carried on on a centralized basis. So this Division now has broad responsibilities for the development of a program, in support of research of a noncategorical nature—noncategorical in the sense that it is as important for one categorical disease as for another—and for the estblishment of a very broad training program for those sciences that, not being categorical, are nonetheless essential for the normal development of the category.

Mr. Denton. But you take allergy and metabolic diseases; they were in this division at one time, were they not?

Dr. Shannon. Yes, sir. Historically, there was an NIH appropriation and a Cancer Institute appropriation.

Mr. Denton. Everything but the cancer institute came out of this Division.

Dr. Shannon. Yes, sir.

And then as a result of the Mental Health Act—this was when, Dr. Felix?

Dr. Felix. 1946 it was passed, but we became an institute in 1949.

Mr. Denton. I think when I came on the committee there was just heart, cancer, and mental health as separate institutes.

Dr. Shannon. But then came the Omnibus Medical Research Act (1950) that made possible the organization of our present institute structure. This Division (DGMS), rather than being a catchall, was set up as a balance for the categorical areas covered by a series of institutes. Then, as the programs in each category evolved more broadly, it became obvious to us, that certain of the more fundamental sciences could be better done on a centralized basis. In net effect, these sciences which were originally in a general appropriation, were distributed to categorical appropriations for development, and were later brought back for central operation.

Now it is true that, in addition to these broad missions, this Division is asked to handle requests on those diseases for which there is not a special base within the categorical institutes.

FUNCTIONS OF THE PROPOSED INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mr. Denton. Now, you propose at this time another Institute of Child Health, and what is the rest of it?

Dr. Hunt. We already have the Center for Research in Child Health, which has been set up by the Surgeon General within our Division.

The proposal is for a new Institute of Child Health and Human Development, for which legislation will be required.

Mr. Denton. I see.

Dr. Hunt. If, as and when an institute is established, some part of our present functions will be moved into it.

Mr. Denton. It takes legislation to do that.

How much of your appropriation of $92 million would be used in this new Institute?

Dr. Hunt. Not a large amount. I would hesitate to make an estimate on that.

Dr. Shannon. We have the figure for research grants, which would be between $1 and $2 million. The overall figure I do not have at the present time.

Mr. Denton. Just what subjects would come under child health, that you have now?

Dr. Hunt. Some part of our developmental biology studies would almost certainly be included in an Institute of Child Health and Human Development.

Some of the work that we are supporting in studies in embryology, studies in cell biology, those that were specifically directed at the growth of the individual human being, would very likely be moved into the new Institute.

Mr. Denton. The Communicable Disease Center down at Atlanta does research on measles, mumps, scarlet fever, and things of that kind. Would you do that work at the new institute?

Dr. Hunt. Little or none, I would expect.

The concept at present is that the new institute will focus upon normal growth and development, and leave the disease aspects of childhood with the other Institutes.

Mr. Denton. I would think those things are children's diseases. What would you do with pediatrics and obstetrics, things like that? Do you deal with them now?

Dr. Hunt. There would be some pediatrics in the sense of the handling of children.

Dr. Shannon. Normal growth.

Dr. Hunt. Normal growth and development.

Dr. Shannon. Emotional development.

Dr. Hunt. Yes, the behavioral aspect of this is expected to be rather heavy.

Mr. Denton. Would you do any work on crippled children there, children recovered from polio, born deformed and things of that kind?

Dr. Hunt. Just how that would be worked in, we do not know at the moment. Some of this would come awfully close to what the Children's Bureau is doing and what they will continue to do.

Mr. Denton. What other aspects of your Division will that embrace?

Dr. Hunt. The proposed new Institute will also include studies of the biological aging process, since this is the other end of the spectrum in growth and development; not the diseases of old age as such, but studies of what happens to humans and other living organisms with the passage of time. It is important to get information along this line before you can adequately treat the diseases of old age superimposed upon the normal aging process.

Mr. Denton. I think that is all, Mr. Chairman.

Mr. Fogarty. Mr. Marshall.

NIH GRANT PROJECTS FOR AGING, 1961 AND 1962

Mr. Marshall. I noticed in your statement, Doctor, that you mentioned that you have 700 grant projects in aging in 1961.

Dr. Hunt. Yes, sir; over 700 research projects in aging.

Mr. Marshall. How many do you expect to have in 1962?

Dr. Hunt. This is a little hard to predict. The number is continuing to go up each year. This, of course, represents research projects being supported by all of the Institutes, not only by our Division.

The Center for Aging Research acts as the focal point for activities in aging, not only for our Division but for the seven Institutes, and the level we will end up at depends on what happens with the programs of eight granting units.

I would expect that there will be an increase in the number of projects in aging, but whether it will be 200 or 300 or 400 is pretty hard to say at this point.

Mr. Marshall. You did not make any estimate, then, as to how many you expected in 1962?

Dr. Hunt. No, sir. This is a retrospective analysis of what actually happens in the field. It is not budgeted for as such. It is simply carried as part of the program of each of the Institutes and of our Division. And after the fact, the Center for Aging Research looks at what all the Institutes have done and tabulates those projects which are thought to be related to aging.

Dr. Shannon. I might say, Mr. Marshall, we have a summary of the aging program that you might like to see. Whether you wish to insert it in the record or not, I do not know.

But this gives some detail of how this program was distributed by Institutes over the past 3 years—1958, 1959, 1960, and for the current year.

I might point out that the importance of the Center on Aging Research and the context in which it operates is that, having surveyed certain areas, it makes known to the Institutes the deficiencies in the programs so that they can guide their actions accordingly. That is one thing.

The second thing is to insure that our institutional grantees are aware both of the magnitude of the problem and of the mechanisms that are available from the National Institutes of Health to support an expansion of their program.

This is a staff agency that in itself does not have a program. In other words, it facilitates the total program of the National Institutes of Health and serves as a point of surveillance and a source of information for planning purposes.

Mr. Marshall. How many of these 700 grant projects that you mentioned, that cost the taxpayers $18 million, will be completed in 1961 and so not be carried over to 1962?

Dr. Hunt. I am afraid we do not have an analysis of that. Most of them are continuing projects, because the study of aging is normally a long, extended kind of research.

Mr. Marshall. Do you have a list of these 700 grant projects?

Dr. Hunt. That is being compiled right now. We should have it available very shortly.

Mr. Marshall. Could you send to me a list of the 700 grant projects?

Dr. Hunt. We shall certainly do that, as soon as it is available.

Mr. Marshall. And the time that they were started and the date that you would expect that they would be terminated. Would you do that?

Dr. Hunt. We can give you the term of each one; yes, sir.

Dr. Shannon. Mr. Marshall, could I interject a point there?

If you mean the date that committed support will be terminated, this we can do.

Mr. Marshall. Yes.

Dr. Shannon. But we would expect that, on balance, these projects are not too different from many of our other projects in broad areas, where we find it desirable, because of the excellence of the work, to continue approximately 85 percent of the projects in any given year.

In other words, they must come up and compete anew for funds and stand on their merits. But in any substantial number of projects one will find that about 85 percent will be continued from one year to the next.

The important thing is that at the end of the committed period, the total progress to that date, together with the work underway at that time, and with the plans for the future, are reassessed in order to determine whether the work warrants continuation.

Mr. Marshall. Well, Dr. Shannon, when you enter into these research grants, do you estimate a target date or goal as to when you may expect termination; do you do that?

Dr. Shannon. There are target dates for the small individual projects contained within a broad program—but they are not really target dates; they are estimates of the time that will be needed to accomplish the project outlined within the grant proposal. But as one goal is obtained by an investigator, or long before that is obtained, parallel lines of investigation are undertaken. So that one is looking at a succession of goals, some of which are accomplished, others of which are determined not to warrant continued investigation. And one has a continuing series of individual programs within the broader objectives of the investigation.

Mr. Marshall. Well, in this information that I would like from you, could you indicate those that have been completed?

Dr. Shannon. We can indicate those that have been terminated.

Mr. Marshall. That would be satisfactory.

Dr. Shannon. Yes, we will do that, sir.

Mr. Marshall. So I will know when I get those lists those that have not been terminated but will be continuing.

Dr. Shannon. Yes, sir.

Now, the ones terminated in this field will be very few, because this is a program that has grown only in the last 2 or 3 years. But this information we will give you, sir.

Mr. Marshall. Thank you.

Thank you, Mr. Chairman.

Mr. Fogarty. I think we will finish with your budget, Dr. Hunt, and then we will go back to the general statement of Dr. Shannon.

ESTIMATES FOR 1961–62

The appropriation for 1961 is $83,900,000; however, activities totaling $7,205,000 are proposed to be transferred to other accounts, leaving $76,695,000. The Eisenhower budget is $87,404,000 or a net increase of $10,709,000, and the budget amendment brings the request to $95,341,000, or a total of $18,646,000 over the 1961 level.

I assume those figures are right.

Mr. Seggel. Yes.

1961 COMPARATIVE TRANSFER TO THE BUREAU OF STATE SERVICES

Mr. Fogarty. Tell us about the transfer of $7,205,000 worth of your activities.

Dr. Hunt. The greater part of that is transferred to the Bureau of State Services for the environmental health activities, which you recall were the subject of discussion in this committee 2 years ago. And following the report of a special committee set up by the Surgeon General last year, it was determined that environmental research grants would be transferred to the Bureau of State Services pending the proposed establishment of a Bureau of Environmental Health, and on July 1 they will take over this activity.

Included within that is a figure of something over a million dollars, which is also going to the Bureau of State Services for accident prevention activities.

HISTORY OF 1962 BUDGET REQUEST

Mr. Fogarty. Give us the history of your 1962 regular request and then the history of the budget amendment.

Dr. Hunt. There were several levels of requests. Do you want us to start with our request to the NIH?

Mr. Fogarty. Yes.

Dr. Hunt. The original estimate for this appropriation to the NIH, including $3,211,000 for biologics standards, was $138,155,000. The preliminary submission by the NIH to the Public Health Service was $104,032,000, including, at this level, $3,050,000 for biologics standards. The submission by the Department of HEW to the Bureau of the Budget was $95,767,000, with the same amount, $3,050,000, for biologics standards.

The budget submitted to Congress by President Eisenhower was for $87,404,000, including $3,025,000 for biologics standards.

Mr. Fogarty. So you went from $138,155,000 down to $87,404,000, is that right?

Dr. Hunt. Yes, sir.

Mr. Fogarty. That is including biologics standards.

Will you develop a statement as to what you wanted $138,155,000 for and how the program will be affected if you do not get it?

Dr. Hunt. We have a statement of what we would use these $138 million for.

The present revised budget would permit us to continue all of our present activities at going levels and, in addition, would permit us to expand clinical research centers, general clinical research centers, from $12 million level to a $13.5 million level and would permit us to increase our research grant activities by $7,681,000.

Mr. Fogarty. Will you put a detailed statement in the record?

Dr. Hunt. Yes, sir.

(The information requested follows:)

1962 original estimate to National Institutes of Health

Grants:	
Research	$88,281,000
Fellowships	12,125,000
Training	32,000,000
Total grants	132,406,000
Direct operations:	
Biologics standards:	
Direct operating funds	2,624,000
Reimbursements	587,000
Total biologics standards	3,211,000
Review and approval:	
Direct operating funds	1,141,000
Reimbursements	852,000
Total review and approval	1,993,000
Administration:	
Direct operating funds	513,000
Reimbursements	32,000
Total administration	545,000
Total direct operations	5,749,000
Total, G.R. & S	138,155,000

HISTORY OF BUDGET AMENDMENT

Mr. Fogarty. What about your budget request for a budget amendment?

Dr. Hunt. The total request in the amended budget is $95,341,000, which includes $3,050,000 for biologics standards.

Mr. Fogarty. What did you ask for?

Dr. Hunt. Our original estimate to NIH last fall was $138,155,000, of which $3,211,000 was for biologics standards.

Mr. Fogarty. That is not the budget amendment.

Dr. Shannon. No.

I can tell you approximately. The budget amendment is approximately $24 million below the requested amount proposed for the budget amendment. We can furnish that figure for the record.

Quite frankly, Mr. Chairman, we have had so many budgets——

Mr. Fogarty. How many budgets are you working with, anyway, on that side of the table?

Mr. **Kelly.** My problem, Mr. Chairman, is that I have a total figure of all the Institutes, I do not have this one.

Dr. **Shannon.** This is particularly hard, because this is part of the series of changes in estimates.

Mr. **Fogarty.** All right, will you provide for the record, in your professional judgment how much should be appropriated.

Dr. **Hunt.** I will be glad to submit that.

(The requested information is included with the Professional Judgment Budget estimates for all NIH appropriations on p. 476.)

BACKLOG OF APPROVED RESEARCH GRANT APPLICATIONS

Mr. **Fogarty.** What will be the total of approved but unfunded research applications at the end of 1961?

Dr. **Shannon.** $5,033,443, if institutional grants are funded.

Mr. **Fogarty.** I am going to ask the same question for each of the Institutes.

Dr. **Shannon.** Yes, sir. We will furnish that for the record.

Mr. **Fogarty.** Do you think you will have any at the end of 1962 if this budget is approved?

Dr. **Hunt.** The revised budget?

Mr. **Fogarty.** Yes.

Dr. **Hunt.** Yes, sir. I expect the amount will probably be at least as large, probably somewhat larger.

(The information follows:)

Estimated 1961 approved but unfunded research grant applications

	Excludes institutional research grants program	Includes institutional research grants program		Excludes institutional research grants program	Includes institutional research grants program
GRS-NIH (DGMS)	−$3,602,443	−$5,033,443	Arthritis	+$842,298	−$1,130,702
Cancer	+896,346	−1,075,654	Allergy	−918,050	−2,208,050
Mental	+1,488,380	+380	Neurology	+658,461	−787,539
Heart	−1,468,389	−3,527,389			
Dental	+503,000	+217,000	NIH, net	−1,600,397	−13,545,397

TISSUE TRANSPLANTS

Mr. **Fogarty.** What research are you doing on tissue transplants?

Dr. **Hunt.** We have a small group of people who have had one meeting and who will be getting together for at least one more meeting to try to develop a plan for attacking this problem in an organized fashion. There are at present a good many research projects in biochemistry and immunology and various other fields which bear on the problem. It would seem to our advisers that it would be useful to try to focus a little more directly on it. We expect that there will be more direct activity.

GENETICS

Mr. FOGARTY. In the field of genetics, what are you doing?

Dr. HUNT. Here again, we have quite a large number of research projects that we are exploring.

Mr. FOGARTY. Anything that is exciting?

Dr. HUNT. That is a difficult question to answer. We think some of it is very exciting, but most of it would not sound very dramatic in a popular publication. Investigators are making progress in understanding the genetics, the background of cell development, which we find very exciting.

Dr. SHANNON. I think the main thrust here is in the development of an understanding of how genetic information is chemically transmitted from one parent to the child; and, more than that, the possibility that we shall be able to modify, chemically, the nucleic acid that transmits this information so as to produce different results.

We are trying to relate specific types of genetic information to specific diseases, on the one hand, and to specific characteristics of invading viruses, such as the polio virus, on the other. I think the whole thrust in this field is toward the understanding of the general chemical basis of the genetic mechanism. And this is very complicated.

The practical application of this to the broad understanding of disease is many years off. In other words, we are now forming the basic foundation for the development—and, hopefully, we shall shortly see the development—of very broad concepts.

Mr. FOGARTY. Now, in layman's language, how could I explain that, if I wished?

Dr. SHANNON. I would say this, that one can grasp the genetic influence if one talks about general diseases of one sort or another in understandable terms; such as congenital heart disease or congenital development of a specific metabolic disease, or congenital predisposition to disease.

It is important that we have an understanding of how the particular particle of germ plasma—that is, the material of the original cell from which the total body is developed—joins up the male and female factors to determine the individuality of the new organism; how the characteristics of the parents are transmuted by the single cell into the characteristics of a wholly new individual.

Primary genetic characteristics are such things as the color of the skin or the color of the hair or the color of the eyes or the blood group of the individual. But there are many transmitted characteristics that are very important in determining the presence or absence of overt disease or the presence or absence of the susceptibility to disease.

The chemical substance that carries the genetic information is the material that is called nucleoprotein, which is a very large chemical entity that will differ from individual to individual depending upon the arrangement of the units that make its complex whole. The units themselves and their arrangement determine congenital disease and susceptibility.

In other words, this is almost coding; it is almost like an IBM card which carries coded information that is less obvious in itself than in the arrangement of its series of holes but which is useless if the code is not understood.

Mr. Fogarty. Please expand on that for the record.

Dr. Shannon. Yes, sir.

(The additional statement requested follows:)

The Promise of Research in Genetics

The human being is a complex physical and chemical structure, every part of which is determined largely by genes inherited from his parents. The characteristics thus formed include not just the color of the child's hair and eyes and his intelligence and temperament, but also his bodily vigor, resistance to disease, and longevity. Not all genes, however, are beneficial. Genes can carry a susceptibility to disease, and actual malformations in the child can result from genetic factors.

The study of genetics therefore is one of the foundation stones upon which all medical and biological research is built. It is not an exaggeration to say that the study of genetics offers the promise of giving man some control over his biological destiny, so that, by influencing the genetic factors, he some day may be able to head off or control many still-baffling diseases, on one hand, and strengthen certain beneficial characteristics, on the other. He also might have a powerful weapon against the genetic defects of radiation which can be transmitted from generation to generation.

To achieve such a goal, scientists need to know the answers to many thousands of questions. These include the material composition of the gene, its exact means of transmission from parent to child, and its mechanism of action. The importance of work in this field is illustrated by the fact that in recent years there have been three Nobel Prizes awarded in genetics, in connection with two components which are thought to act like genes and which may carry the genetic "blueprint" for the developing child. (These are nucleic acid molecules, ribonucleic acid and deoxyribonucleic acid with the short names, RNA and DNA.) Many hundreds of scientists are at work trying to determine how the blueprint works, whether or not it can be modified, and, if so, how.

In closely related research effort, scientists are studying how the blueprint factor reproduces itself, how the division of cells transmits genetic material from cell to cell. Scientists also want to know more about the relationship between specific diseases and specific genetic factors. For example, they want to know how an invading virus, such as polio, is affected by its victim; and they want to know what effect the polio virus may have on the victim's genetically determined characteristics. In the study of the way cells change, much more information is needed to be able to distinguish spontaneous change from, say, that resulting from radiation.

Most of the research mentioned thus far pertains to work at the level of the large molecules and cells—work crucially important in attaining a basic understanding of human reproduction and development.

In other genetic research, of equal importance, scientists are studying the effects of the genes upon blood, and upon tissues and organs—as in connection with the very significant work and unsolved problems in transplanting tissue and organs.

Man thus is entering an entirely new realm of understanding about human biology and its relationship to disease, with the prospect in years to come of achieving and maintaining greater health than ever before imagined.

ANESTHESIOLOGY

Mr. Fogarty. What about anesthesiology?

Dr. Hunt. This is a field in which we are supporting some research and some training. The research aspects of it have to do with developing anesthetic agents and anesthetic techniques which will provide greater safety than we now have in giving anesthesia for operations.

Mr. Fogarty. That is all done by a specialist, is it not, today?

Dr. Hunt. Anesthesiology is a medical specialty, yes. And our programs involve training as well as research in order to train more young physicians in this field.

NURSING RESEARCH

Mr. Fogarty. What are you doing in nursing research?

Dr. Hunt. We work very closely with the Division of Nursing in the Bureau of State Services. There is now research to the extent of over $1 million a year in nursing, which is funded from this appropriation.

TESTING LIVE POLIO VACCINES

Mr. Fogarty. In your Biologic Standards Division you have a testing program for live polio vaccines.

Dr. Shannon. Yes, sir.

Mr. Fogarty. How are you making out?

Dr. Shannon. Well, the program is coming along very well from the standpoint of testing—for developing laboratory tests that will reflect the efficacy of the vaccines. The problem here is that the live polio vaccine contains a virus which is derived from what otherwise is apparently normal kidney tissue. So that in testing the vaccine, one can demonstrate, not infrequently, the presence of two viruses.

Now, this contaminating virus can be destroyed by a variety, or combination, of heat and chemical means. But this is a very complex procedure that to some extent lowers the potency of the polio virus. And while the simian virus, the virus of monkey origin, cannot be shown to be a pathogen that has caused disease in humans, it still represents a complication in the development of a vaccine.

It is our feeling, in the absence of an ability to develop a virus vaccine which contains only those viruses that one wishes it to contain, that we do not have available at this time a general manufacturing technique for large-scale production.

Mr. Fogarty. When do you think you will be in a position to license manufacturing?

Dr. Shannon. Well, it would be our guess, licensing probably not before this summer or production before this fall. That is our estimate.

Mr. Fogarty. Do you think you will be at that point then?

Dr. Shannon. I hope so; yes, sir.

MEASLES VACCINE

Mr. Fogarty. Tell us about the immunizing agent against measles?

Dr. Shannon. Well, this is a totally new development in terms of the possibility of developing a product for human use.

But the work itself goes back to very early work by Stokes of Philadelphia and Enders of Boston. I would say that was begun in the late forties. There are a number of viral agents that have been derivable from measles and have been grown and have shown the ability to transmit the disease.

The main advances have come from the demonstration that, as with the polio virus, the measles virus can be grown very readily in tissue culture. This was shown very well in the early fifties. It was also demonstrated that for certain of the viruses, one can reduce their ability to introduce disease in a human; that they can be given to humans without the production of disease and yet stimulate those antibodies that will in turn destroy measles virus introduced at a later date.

The problem up to the present time has been a problem of how one works with this virus in the laboratory. The most natural host for studies is the monkey. But it now turns out that most of the monkeys that have been introduced for study work in this country from India already have the measles antibodies. It seems likely, from studies during the past 6 to 9 months, that these monkeys have had human contact and have, in fact, developed measles as a disease or at least have developed the infection and that the antibodies come from the measles virus.

This was surprising. It is not generally widespread in the very young, but is almost inevitable in the old, and it is not found in those monkeys that do not have contact with the human—such as the green monkey in Africa—but is very common in the macao of Africa, where the monkeys are very closely intermixed with the human population. The ultimate development of this vaccine must await (1) the development of resources of clean monkeys in adequate amount to test for infectivity and antibody production; and (2) the ability to be certain that this virus, as in the case of the polio virus, can be developed as an attenuated strain of live measles vaccine, without contaminating strains of viruses of monkey origin that impair the purity as well as potency.

But this will probably develop much more rapidly than is the case with the polio vaccine, because the ordinary laboratory monkey is such a very superior test object that a lot can be done with a normal monkey that, in the case of polio, has to be done with a human.

I would expect, in the case of the measles vaccine, that perhaps in a year and a half this should be available for distribution. That is a rough estimate. And this is something with which we can break the bottleneck.

WORK OF BIOLOGICS STANDARDS UNIT

Mr. Fogarty. Is the biologics standards work not enough different from the work done under the Division of General Medical Sciences that the two should be set out as separate appropriations?

Dr. Shannon. Well, at the present time they are the residual programs that are still contained as operating programs within the general appropriation of the National Institutes of Health.

We have recommended that serious consideration be given to setting out to the Division of General Medical Sciences a program in parallel with our Institutes, because it has, except for the absence of direct operation, all the functions of an institute and requires the total services of an advisory council in precisely the same manner the other Institutes do.

FELLOWSHIP AND TRAINING PROGRAMS

Mr. Fogarty. I notice several places in connection with your fellowship and training program such quotes as these:

> These awards also help * * * in meeting the needs for additional faculty members in the shortage fields. * * *

That is on page 23 of your justifications. And on page 25, you say:

> General research training grants program has been designed to meet * * * the increasing need of the Nation's medical schools for academic personnel. * * *

Is this program tending to become more and more a program of general aid to medical schools to help them build up the faculties?

Dr. HUNT. It is not a general aid program. It does help them build up faculties in specific areas, because when they have a training program in, let us say, the anatomical sciences, part of the training grants awards do usually go to pay the salary of one or more additional staff personnel who are spending most of their time in training and research.

Mr. FOGARTY. Well, it is indirectly, is it not?

Dr. HUNT. Yes, sir.

Mr. FOGARTY. It looks pretty direct to me, but——

Mr. LAIRD. We hear a lot about "back door" financing—this is "side door."

Dr. HUNT. Yes, it has very little effect on undergraduate teaching programs. It focuses on the graduate program.

Dr. SHANNON. The research training grants program supplies the additional skills that indirectly benefit the teaching program of the Department, even though these skills are primarily addressed to the problems of research and research training. We cannot expand the skills of the Department without being, broadly, beneficial to all of the functions of the Department.

PROJECT TITLES

Mr. FOGARTY. Doctor, it is difficult for us on this committee that believe in these programs, when someone questions us on the merits of an individual project and quote from an editorial or read from a magazine or a newspaper article ridiculing the project. Last year two or three were mentioned. Generally, they seemed to be in the mental health field.

What about this one on cocktail parties? Do you want to answer that?

Dr. SHANNON. That is in the mental field?

Mr. FOGARTY. I thought you ought to comment on it in general, because it is awfully difficult for any of us, as laymen, to get up and explain the necessity for some of these. We cannot possibly be acquainted with each of the thousands of projects.

I remember 7 or 8 years ago there was quite a lot written about a few of your projects. I think they were unfairly written up in the newspapers. But if someone wants to do a job on this kind of a program the usual procedure is to pick out an example or two and try to ridicule it to death.

Dr. SHANNON. I would like to comment on the thing in general.

This does happen to be in the mental health field, and I think we have someone who can give you the general background on the field of study. Both Dr. Felix and I have detailed information on the programs in this project and on what was done in the totality of the grant.

But the problems we face relate to the way information of this sort becomes generally available. Now, our problems up to about 4 or 5 years ago stemmed primarily from the problems of titling. I do not think we were careful enough to be certain that the title was generally descriptive of the substance of the work that was being done as opposed to having a trivial title that satisfied the limited needs of the investigator or told precisely how he planned to do a thing. We have paid particular attention to that, and I think we have titles now which are purely descriptive of the work that is done.

PROFESSIONAL JUDGMENT BUDGET FOR 1962

Mr. FOGARTY. Dr. Shannon, when the Surgeon General was here, we told him that we wanted you to be prepared to present to the committee each of the budgets that you have presented to the Surgeon General, that he has presented to the Department, that it has presented to the Bureau of the Budget, and a professional judgment budget like that we requested last year. We will place these in the record at this point, along with other pertinent data relating to the budgets presented to Congress.

Dr. SHANNON. We will do that.

(The requested information follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
April 14, 1961.

Hon. JOHN E. FOGARTY,
Chairman, Subcommittee on Labor, Health, Education, and Welfare, House Appropriations Committee, Washington, D.C.

DEAR MR. CHAIRMAN: The professional judgment budget estimates from the National Institutes of Health are submitted with Dr. Shannon's comments for insertion in his testimony.

I would like to emphasize that these estimates were made by the individuals without any guidelines or supervision from this office or from the Office of the Secretary.

As pointed out by Dr. Shannon, these estimates do not constitute in the aggregate a National Institutes of Health or Public Health Service budget proposal. They do not take into consideration those overall factors normally influencing the construction of a budget proposal.

Sincerely,

LUTHER L. TERRY, *Surgeon General.*

SUMMARY OF PROFESSIONAL JUDGMENT BUDGETS

In response to your request, Mr. Chairman, I am submitting for the record a series of estimates for 1962, prepared by the individual Directors of the several Institutes and program Divisions of the National Institutes of Health, which reflect their best professional judgment of the funds which could be used for their individual programs. These include both projections for operating programs and proposals for additional construction.

These estimates have not been influenced through guidelines or review such as occur in the normal budgetary process and, accordingly, do not represent in the aggregate an NIH budget proposal. Consideration has not been given to those factors normally influencing budget proposals such as—

1. The consistency of the proposals of individual Institutes with existing congressional directives and legislation.
2. The appropriateness of relative emphasis among programs as for example between research grants and training grants.
3. The adequacy of manpower, space, and other resources when the total budgets of all Institutes are added up.
4. The effect of combined Institutes proposals upon educational institutions.

5. The sum total of all proposals in relation to fiscal feasibility and other broad policy considerations.

6. The effect of projected program increases upon the Central (NIH) Management requirements.

National Institutes of Health, Mar. 28, 1961

1962 professional judgment budget estimate (in thousands)

OPERATING APPROPRIATION

	Total estimate
Grants:	
Research	$470, 855
Fellowships	34, 288
Training	139, 638
State control programs	16, 500
Community demonstration projects	3, 000
Total grants	664, 281
Direct operation:	
Research	[1] 69, 920
Biologics standards	3, 125
Review and approval	12, 332
Training activities	700
Professional and technical assistance	29, 085
Chemotherapy contracts	25, 000
Administration	3, 765
Total direct operations	143, 927
Subtotal, operating appropriation	808, 208
CONSTRUCTION	
Division of Biologics Standards—experimental animal and refrigerated storage facilities	2, 160
Construction of cancer research facility	12, 000
Heart—nonmatching construction grant for gerontology in Baltimore, Md	12,000
Allergy—Rocky Mountain Laboratory	650
Total	835, 018

[1] Includes $800,000 for expansion of NINDB Laboratory of Perinatal Physiology, Puerto Rico, including construction.

General Research and Services, Mar. 21, 1961

Fiscal year 1962 professional judgment budget

Activities	*Total estimate*
Grants:	
Research projects	$87, 568, 000
Research fellowships	13, 015, 000
Training	39, 250, 000
Total grants	139, 833, 000
Direct operations:	
Biologics standards	3, 125, 000
Review and approval	2, 020, 000
Administration	542, 000
Total direct operations	5, 687, 000
Total estimate	145, 520, 000
Research projects:	
1961 program (exclusive of environmental health grants)	28, 615, 000
1962 commitments (85 percent of 1961)	24, 330, 000
Backlog of approved but unpaid applications, end of fiscal year 1961	4, 474, 000
1962 supplements (8 percent of 1961)	2, 289, 000
1962 new projects	23, 513, 000
Subtotal	54, 606, 000
Institutional research grants (10 percent of 1962 program)	6, 068, 000
Subtotal	60, 674, 000
Special program grants:	
Scientific evaluation and planning grants	848, 000
International medical research	500, 000
General clinical research centers (see separate projection)	25, 546, 000
Subtotal	26, 894, 000
Total need for 1962 (at 15 percent overhead)	87, 568, 000

At the close of 1961 it is predicted that there will be a backlog of approved but unpaid research projects approximating $4,474,000. On the basis of experience from the past several years it may be predicted that regular new grant applications recommended for approval by the advisory groups will reach at least $23,513,000 for 1962, an increase of 30 percent minimum in new applications over 1961.

These increases will be devoted primarily to fundamental biomedical research in such fields as biochemistry, genetics, cell biology, physiology, embryology and development, to public health problems, including nursing and epidemiology, and to projects in allied fields. In addition, emphasis will be directed toward a number of emergent research areas warranting increased consideration because of their pressing and timely importance to the development of contemporary biology and medicine. These include studies of aging, biomedical engineering, histocompatibility, research in comparative anatomy, developmental biology, and projects which are relevant to several of the categorical Institutes and the Division of General Medical Sciences.

The projected requirement for general research grants for 1962 of $87,568,000 is a realistic projection based on experience and on an accelerating expressed need for support of research in the general medical sciences. This projected requirement represents an increase of $34,244,000 over the 1962 revised estimate.

General clinical research centers:

1961 program	[1] $8, 000, 000
1962 commitments	8. 000, 000
Backlog of approved but unpaid applications, end of fiscal year 1961	5. 046. 000
1962 supplements	500. 000
1962 new projects	12, 000, 000
Total need for 1962 (at 15 percent overhead)	25. 546, 000

[1] Includes the $3,000,000 funded by 6 of the Institutes for this program and administered by this Division.

At the close of 1961 the backlog of approved but unpaid general clinical research center applications will be approximately $5,046,000. The total of committed continuations of the 20 grants in force at that time will be approximately $8 million. The supplemental requests are expected to exceed $500,000. The sum of these three needs ($13,546,000) exceeds the revised estimate level of $13,500,000, which is, therefore, a maintenance budget that will not allow the establishment of any new general clinical research centers.

It is predicted that the three council meetings of 1962 will result in 24 approved applications at the present average level of $500,000 each. The support of these new programs will need approximately $12 million in addition to the $13,500,000 in the revised estimate, or a total of $25,546,000.

This $12 million increase will permit the establishment of 24 new clinical research centers in leading medical schools and research hospitals. There is urgent need for increased investigation of human diseases by direct research on patients under scientifically controlled and safe conditions. These new centers will also permit the accelerated investigation of the applicability of results from laboratory and animal research to the diagnosis and treatment of human disease.

Research fellowships:

1961 program		$10, 100, 000
1962 increases		2, 915, 000
Predoctoral:		
Full time	$3, 000	
Part time	1, 000	
Postdoctoral	875, 000	
Special	196, 000	
Senior:		
Regular	1, 000, 000	
Career research professorships	500, 000	
Foreign	340, 000	
Total need for 1962		13. 015. 000

Additional funds for this program will be used to expand the opportunities for intensive research training of candidates in the fundamental biomedical and other health-related sicences in such shortage areas as medical genetics, physiology, molecular biology, and experimental pathology.

The total requirements estimated for 1962 of $13,015,000 represent an increase of $2,915,000 over the 1962 revised estimate of $10,100,000. Approximately $4,400,000 is required for the regular fellowship program to support increased numbers of candidates and to encourage others in future years to elect careers in the fundamental fields of the biological sciences. An additional $1 million is requested for the senior fellowship grant program, bringing the annual support of this program to $5,500,000. This will permit the continued growth of this successful program in 1962 to help relieve the shortage of researchers and teachers trained in the basic sciences and to aid these scientists in developing their own potential in research work. Approximately 75 additional senior fellows can be supported in 1962 with this increase.

Training:	
1961 program	$25, 500, 000
Adjustment of beginning dates in 1961	1, 500, 000
Total 1961	27, 000, 000
1962 commitments	25, 500, 000
Approved but unpaid applications end of fiscal year 1962	4, 750, 000
1962 new projects	9, 000, 000
Total need for 1962	39, 250, 000

The total requirements for 1962 of $39,250,000 represent an increase of $12,750,000 over the 1962 revised estimate of $26,500,000. This increase is based on the large number of high-quality applications received from basic science departments of the medical and graduate schools and recommendations of the training committees, composed of non-Federal experts in the basic science fields, and the National Advisory Health Council.

At the end of 1961, it is estimated that approximately $4,750,000 of approved applications cannot be paid from 1961 funds. The $9 million for new projects in 1962 represents estimated approvals of $6 million in research training grants, $1,500,000 for continuation and expansion of current medical student research training programs and $1,500,000 for initiation of wholly new programs.

The increase in research training grants will be used to give added emphasis to the areas of (1) biophysical sciences, (2) development biology, (3) genetics, (4) biomedical engineering, (5) biomathematics, (6) comparative pathology, and the (7) behavioral sciences.

Biologics standards

The Division of Biologics Standards occupied its new building during 1961 and although nonrecurring money ($54,000) was appropriated for alterations and renovation, all necessary adjustments could not be accomplished. In the process of moving, it became apparent that further laboratory alterations were called for in order to make maximum use of the building. This is particularly true in connection with the program demands of research and testing for both live poliomyelitis vaccines and measles vaccines. For this purpose, $50,000 is being requested.

In connection with the accelerated live vaccine programs, where additional numbers of monkeys are being used for testing, the Division is required to purchase caging equipment ($10,000) and more adequate pathology laboratory equipment ($15,000).

The total estimate of $3,125,000 represents an increase of $75,000 over the 1962 revised estimate.

Review and approval

Fourteen additional positions will be required to administer the expanded noncategorical research project grants program and research training programs. This is an increase of $134,000 for personal services and related costs over the 1962 revised estimate.

Administration

An increase of seven positions and $61,000 over the 1962 revised estimate will be required for the overall planning, direction, and coordination of the programs of the Division of General Medical Sciences and the center for aging research, which directs a program designed to stimulate research in the field of aging.

EXPERIMENTAL ANIMAL AND REFRIGERATED STORAGE FACILITIES FOR BIOLOGICS STANDARDS

March 17, 1961

The provisions of the Public Health Service Act require that the Secretary HEW issue establishment and product licenses to establishments to engage in the manufacture of biological products "only upon a showing that the establishment and the products for which a license is desired meet standards, designed to insure the continued safety, purity, and potency of such products." The Division of Biologics Standards has been designated as the organization within the Public Health Service to administer the provisions of the Public Health Service

Act pertaining to biological products. In order to fulfill its obligations in connection with this administration the Division has developed a sound control program augmented by a well-rounded research program. This concept of the Division's activities has been accepted, and in fact endorsed, by all levels within the Government including the Congress.

The products involved in the work of this Division are complex and are derived for the most part from pathogenic or potentially pathogenic micro-organisms. The testing of these products is also complex since much of this testing must be carried out in living biological systems. Many of these tests are carried out using various animals since it is obviously impossible to conduct such tests in man. Although many of the tests are performed through the use of tissue culture and other laboratory procedures, in the final analysis the testing of the product in a series of living animals is the critical evaluation.

In the development of standards and of control testing procedures for new and established biological products the research program plays a vital part in this process. In the search for meaningful and reliable tests from which can be developed criteria for standards for safety, purity, and potency, a large number and variety of animals are used. Even after a product is licensed, the continuing testing of repetitive individual lots for release purposes by the control program requires tremendous numbers and variety of animals.

As an indication of the size and scope of this aspect of the total Division program, during fiscal year 1960 the following number of animals were used:

Mice	136, 000	Monkeys	2, 800
Rats	3, 000	Hamsters	7, 100
Guinea pigs	12, 700	Chicks	11, 000
Rabbits	4, 100		

In addition it must be emphasized that certain of these animals require special handling and separation because of the nature of the animals involved (monkeys must be separated either individually or in small groups as well as by room to prevent cross-infections). Others require separation because of the nature of the test (rabbits used in pyrogen tests require a precisely controlled temperature environment and isolation from disturbances or sources of excitement). Other animals require separation or semi-isolation because of the product undergoing test (animals used in testing live poliomyelitis vaccine must be separated from those used in evaluating killed polio vaccine and adenovirus vaccine). In addition, in order to obtain valid results from control testing, many such animals must be segregated from all animals involved in the research program since the latter may be used for a variety of experimental situations which may be unknowingly hazardous to the results of control tests carried out in the same area or room.

In the fall of 1960 the Division moved into its new laboratory building. The facilities within this building are excellent for laboratory purposes but can only to a limited degree accommodate the animals now required to meet research and control needs. During the planning and construction phase of this new laboratory building it became apparent that the needs of the DBS program for physical facilities were in excess of those provided for by the new building, additional space of approximately 4,246 square feet in another building is now being used on a temporary loan basis. This deficiency was noted in the NIH report on plans for orderly implementation of the recommendations of the Secretary's consultants on medical research and education (Bayne-Jones Committee). At that time it was envisioned that two annexes to the new building would be needed to provide animal space and that they would be completed by 1966. Unanticipated relocation of utility connections during the course of construction of the DBS building and changing the plans for roads from the locations originally projected now make the original sites considered for the two annexes unsuitable for this purpose. In addition the need to capitalize on progress in the rapidly developing areas covered by the programs of the Division, such as virology, and the need to meet the additional requirements for testing new immunizing agents, such as live poliovirus vaccine and measles vaccines, have further emphasized the inadequacy of the animal space available to meet more than a fraction of projected demands and made more imminent the need for additional space. A reassessment of these needs and of the available locations of experimental animal quarters has led to the conclusion that the need could most readily be met by one building erected immediately adjacent to the present DBS building but on the west side instead of the south side.

An additional deficiency in the physical facilities available to this Division brought about by the increasing number and bulk of test samples, research materials, and of standard preparations is the lack of adequate refrigerated storage space. The Division's programs require space for bulk storage of large quantities of biologics materials at various temperatures including storage for many years of control samples of manufactured biological products for purposes of legal and control reference. Due to the increased activity in live virus vaccines the need for a sizable area devoted to the bulk storage of these materials under refrigeration is imperative. The proposed location and design of this projected building for animal quarters are ideal for including in the construction provision for such storage facilities. It is proposed that approximately one-half of the basement would be used for such facilities. Of this space approximately two-thirds would be constructed to operate at 4° to 10° C., approximately one-sixth to operate at —10° to —20° C. and approximately one-sixth to operate at —60° to —80° C. storage. At present the Division has no bulk storage space in the —60° to —80° C. range. The need for such storage is emphasized by developments in the field of microbiology during the past 2–3 years. Such a facility is urgently needed in connection with the expanding work with live virus vaccines. Its primary need is to preserve material in an unchanged state of activity for a great many years. Since the small amount of space available at —10° to —20° C. and 4° to 10° C. which can be used for bulk storage by the Division is now filled to capacity, additional space in these temperature ranges is also urgently required. It is of extreme importance that this refrigerated storage space envisioned in the proposed new building be provided as soon as possible. Until such is available temporary expedients will be used to meet the problem.

The proposed new construction is envisioned as a facility to house animals undergoing control testing and research experimentation and should not be viewed as an animal holding or conditioning facility. These animal facilities must therefore include many features not required for space used for routine holding and conditioning of animals. For instance, each room must be provided with a basic laboratory bench and a set of services (air, gas, and vacuum) as well as a sink with hot and cold water. These facilities will be used by scientific personnel in their work with the animals in the room. In addition, autopsy rooms must be provided on each floor, since adequate post mortem examination is a vital part of animal testing in both the control and the research programs. Since it will be necessary to protect to the greatest extent possible the integrity of the tests and experiments, several autoclaves, large enough to accommodate a complete rack of cages, will be required. It is also envisioned that some of these rooms both individually and in groups will be especially designed in the interests of safety as isolation suites to provide for work with highly virulent pathogenic agents. The word safety as used in relation to these facilities must be construed as (1) safety to personnel, (2) safety to animals being used on other tests, (3) safety in the sense of being sure that test results are not affected by other tests being conducted in the building. So as to control dissemination of fectious agents within the building as much as possible 100 percent no return air conditioning must be used. These unique requirements, which indicate the very special nature of this building, establish it as an actual extension of the DBS building rather than as merely an animal holding or conditioning facility.

The acquisition of these additional facilities is of prime importance if the Division of Biologics Standards is to continue to operate at the level of competence expected by the Service, the Department, and the public. In the report on the 1960 appropriation bill the Committee on Appropriations of the Senate expressed its attitude toward this Division's program as follows:

"The other major program encompassed within this general appropriation is the Division of Biologics Standards. Congress has given recognition to the importance of this Division by providing it with a new laboratory building, which will be completed and occupied during the first half of the fiscal year 1960. The committee recognizes that the Division carries a tremendous responsibility in its assurance of the safety and effectiveness of biological products. This regulatory function cannot be carried out effectively in the absence of a strong and paralleled research activity. The Division of Biologics Standards has made outstanding research accomplishment. Its findings include discovery of a new antibody for a human blood factor of potential use as a diagnostic tool; development of a test-tube potency test for polio vaccine; a new method for distinguishing virulent from attenuated polio viruses without the use of live monkeys; studies of a photodynamic method of inactivating viruses; and studies of viruses and cancer producing new information of value.

"Because the work of this Division ranges a broad front, involving vaccines and antitoxins, therapeutic serums, and human blood and its derivatives, and because this front is one of rapid and constantly changing discovery and development, the activity is one of significance to the American people. By its action, the committee expresses its confidence in this program and its belief that it must have all of the resources it needs to carry out its complex mission."

The National Institutes of Health have made a preliminary estimate of the cost of construction of this building. The estimate is based on a five-story building, approximately 157 by 60 feet, four stories above ground and one below, with the basement connected to the existing DBS building by a tunnel. The architectural and structural characteristics would be consistent with the existing DBS building. A summary of this preliminary estimate is set forth below:

I. Basic cost of building:			
(*a*) Building (less air conditioning and elevators)		$900, 000	
(*b*) Elevators		190, 000	
(*c*) Air conditioning, 400 tons at $1,200 per ton		480, 000	
Total basic cost of building averaging $33.33 per gross square foot			$1, 570, 000
II. Specialized equipment costs:			
(*a*) Autoclaves, 3 at $40,000 each		$120, 000	
(*b*) Cagewashing:			
New unit	$60, 000		
Relocate existing unit	10, 000		
		70, 000	
(*c*) Refrigeration facility (walls, insulation and equipment):			
300 square feet, −60° to −80° C	180, 000		
300 square feet, −10° to −20° C	100, 000		
1,800 square feet, +10° to +4° C	120, 000	400, 000	
Total cost of specialized equipment			590, 000
Total cost of building and equipment			2, 160, 000

NATIONAL CANCER INSTITUTE

1962 estmates prepared on basis of professional judgment of Institute Director

Activities	*Total estimate*
Grants:	
Research grant programs	[1] [2] $83, 956, 000
Research fellowships	3, 700, 000
Training	10, 845, 000
State control programs	3, 500, 000
Community demonstrations	3, 000, 000
Total grants	105, 001, 000
Direct operations:	
Research	15, 527, 000
Review and approval	2, 044, 000
Professional and technical assistance	10, 392, 000
Chemotherapy contracts	[1] 25, 000, 000
Administration	731, 000
Total direct operations	53, 694, 000
Total estimate	158, 695, 000

[1] Reflects $1,300,000 transferred from grants to chemotherapy contracts during 1961.

[2] Includes $1,000,000 made available in 1961 for diagnostic grants, contracts, or direct operations: in 1962 it may prove desirable to finance some of these activities under contracts or as direct operations. If so, funds would be transfreed to professional and technical assistance during the year.

CONSTRUCTION

Construction of a cancer research facility	$12, 000, 000

Research grant programs, $83,956,000

This estimate provides for an increase over the revised budget of $6,051,000 for general research projects. This will permit payment of 100 percent of the estimated new grants to be approved. It also provides an increase of $2,103,000 for the institutional research grants program, bringing this activity to a level of 10 percent of funds available for research projects.

This estimate assumes payment of indirect costs to be 15 percent of the basic grant. The amount should be adjusted upward if a higher indirect cost amount is to be provided.

The estimate for programed grants in chemotherapy of $6 million is $1,300,000 less than that shown in the revised budget. A corresponding increase is shown in chemotherapy contracts. This reflects a change in types of work to be supported which becomes necessary in 1961 but too late to be reflected in the base figures in the 1962 budget.

This estimate provides an increase of $20 million for cancer construction grants. Space shortages are hampering progress in cancer research. These shortages are not being met by funds made available on a matching basis through the program for construction of research facilities. This is true because of a combination of factors relating to priorities given to cancer facility construction, locally and by national advisory groups. The increase of $15 million over 1961 and $20 million over 1962 revised budget reflects our appraisal of minimum needs for cancer research next year. How this need should be met and its relationships to the general research construction program is an open question.

The estimate for cancer research centers of $11,500,000 is an increase of $4 million over the revised budget.

The center program of the National Cancer Institute will be broadened to include centers for (1) radiation research and training, (2) carcinogenesis studies, (3) human population laboratories, and (4) possibly animal supply. It also may be desirable to increase the use of center-type support for large cancer institutions already in existence.

Research fellowships, $3,700,000

This estimate represents an increase of $1,300,000 over the revised budget for increasing the supply of research manpower. Included in this increase is $500,000 for postdoctoral and special fellowships to provide advanced or specialized training for research, $350,000 for senior fellowships to encourage and support the development of professional personnel for academic and research careers, and $450,000 for career professorships to establish additional full professorial positions.

Training, $10,845,000

This estimate provides for an increase of $3,790,000 over the revised budget. It would provide $2,615,000 for graduate training grants to institutions for the conduct of training aimed at increasing the number of investigators in fields pertinent to cancer research. Teaching grants would be increased $1,175,000 to permit increased payments to schools—payment to 4-year medical schools and osteopathic schools would be increased from $25,000 to $35,000; payment to 2-year schools and dental schools would be increased from $5,000 to $10,000. One new school would also receive these funds. It should be noted that the current level of payments has not been changed for many years.

Community demonstration projects, $3 million

The initiation of the community cancer demonstration project grant program during fiscal year 1960 has received a widespread and effective response. Guidelines for projects that offer the best current opportunities for effective demonstration have been developed and widely disseminated. Because of the current potential to eliminate deaths from cervical cancer, projects to increase the number of women receiving cervical cytology and related examinations have been emphasized. An increase of $1 million for this purpose will permit the continued support of demonstration projects already underway as well as the initiation of new projects in areas that promise to further reduce disability and death from cancer.

Research, $15,527,000

We have recently had a group of experts study our needs in radiation therapy. They have recommended and the Institute agrees that our equipment in this laboratory must be augmented and modified if we are to continue to progress in this field. The increase of $750,000 is for this purpose.

Review and approval, $2,044,000

This estimate includes an increase of $299,000 over the revised budget to cover the cost of reviewing the larger volume of grant applications and $345,000 for reimbursement to the "National Institutes of Health management fund" for services furnished centrally.

Professional and technical assistance, $10,392,000

This estimate includes an increase of $2,761,000 over the revised budget.

An increase of $511,000 in field studies would bring the total for this activity to $3,500,000 of which $500,000 is for carcinogenesis studies, $500,000 for biometry studies, $1 million for epidemiology studies, and $1,500,000 for diagnostic research. In addition $1 million budgeted under grants and originally made available for grants, contracts or direct operations in 1961 may be shifted to this activity during 1962 for diagnostic contracts. This matter is now under study.

An increase of $200,000 would provide additional personnel and support for planning and control of the increased chemotherapy program.

An increase of $2,050,000 is for the virus program. The intent is to supply materials and services to virologists engaged in cancer research. The National Advisory Cancer Council has urged that this be done, for it is believed that by so doing, progress in this field will be greatly accelerated.

Chemotherapy contracts, $25 million

This estimate reflects a change of $2,462,000 over the revised budget. Of this amount $1,300,000 reflects the recent shift of funds from chemotherapy grants.

The program increase of $1,162,000 would provide for increased research costs in ongoing programs and a large program designed to speed the rate at which anticancer agents become ready for trial in man.

Administration, $731,000

The estimate includes an increase of $70,000 over the revised budget to strengthen the overall administration, direction, and planning of the diversified programs of the Institute.

NATIONAL CANCER INSTITUTE—CONSTRUCTION

Construction of a cancer research facility, $12 million

To be included in the professional judgment estimates of the National Cancer Institute is $12 million for the construction of a cancer research facility. The 1961 appropriation provided $700,000 for planning this facility.

At the present time, professional personnel are located in nine buildings at NIH, in Bethesda, and in Silver Spring. Laboratory and office space is needed for existing and new programs, particularly in collaborative areas. The acceleration given to the Institute's programs in the 1962 revised estimates has intensified the Institute's need for additional space, and construction should start as soon as possible.

MENTAL HEALTH ACTIVITIES

1962 estimates prepared on basis of professional judgment of Institute Director

	Total estimate
Grants:	
Research	$50,019,000
Fellowships	5,240,000
Training	37,300,000
State control programs	8,000,000
Total, grants	100,559,000
Direct operations:	
Research	10,165,000
Review and approval of grants	2,425,000
Training activities	300,000
Professional and technical assistance	3,153,000
Administration	965,000
Total, direct operations	17,008,000
Total estimate	117,567,000

GRANTS

Research.—Increase of $13,539,000.

Projection of recommended grants

1. Continuation and supplemental requirements	[1] $27,988,000
2. New grants, including carryovers	15,236,000
3. Subtotal	43,224,000
4. Institutional research grants	5,002,000
5. Indirect costs effective January 1, 1962	248,000
6. Clinical research centers	1,000,000
7. International medical research	500,000
8. Scientific evaluation and planning grants	45,000
9. Total, research	50,019,000

[1] Assumes programing of $1,820,000 in 1961 requested on Mar. 9, 1961.

Of the total of $43,224,000 for the normal programs, $11 million is for the psychopharmacology program, $10 million for the mental health project grants (title V) program, and $22,224,000 is for the regular programs.

The anticipated growth pattern of the clinical research center program, for which funds were first made available in 1961, is such that it is anticipated that the funds required will increase substantially in the second and subsequent years. An increase of $500,000 for financing such centers is considered to be minimal.

Fellowships.—Increase of $2,850,000.

Projection of recommended grants

1. Predoctoral	$2,340,000
2. Postdoctoral	1,170,000
3. Special (regular)	780,000
4. Special (career investigator)	330,000
5. Senior	320,000
6. Career research professorships	300,000
Total	5,240,000

A significant percentage of the increase would be used to permit the payment of approvals unpayable in 1961. This amounts to $600,000: in predoctoral, $300,000; in postdoctoral, $120,000; in special, $180,000.

Based on experience of the last 3 years the projection of increase for 1962 would serve to meet the needs for expanded programs in 1962.

Projection of recommended grants, 1962

1. Continuation requirements	$28,356,000
2. Supplements and expansion of continuing program	3,600,000
3. New program	5,344,000
Total, projections	37,300,000

Program analysis, 1962

Undergraduate	$4,965,000
Graduate:	
General practitioner	4,500,000
Research training	5,750,000
Special areas	1,200,000
Pilot projects, institutes, and conferences	1,800,000
Regular programs	19,085,000
Subtotal, graduate	32,335,000
Total training	37,300,000

State control programs, increase of $2 million

Recent evidence indicates that comprehensive community mental health facilities can prevent a significant proportion of admissions to mental hospitals and also make it possible to discharge many hospitalized mental patients to the community. Among the factors responsible for the increased effectiveness of community mental health programs are the "tranquilizing" drugs, outpatient psychiatric clinics, psychiatric units in general hospitals, aftercare of ex-mental patients by social workers or public health nurses, and the increasing involvement of general practitioners in the treatment of mental illness.

Besides developing new mental health programs in communities, there are also pressing current needs for pilot projects, demonstrations, and evaluative studies to try out and test new methods and techniques suggested by research findings, and to help support the development of mental health services for the social problem areas such as aging, alcoholism, juvenile delinquency, and mental retardation.

At the $8 million level, the minimum grant to a State would be raised from $40,000 to $50,000.

DIRECT OPERATIONS

Research, increase of $475,000

Basic research, increase of $200,000.—An increase of $50,000 and seven positions is requested for the Addiction Research Center to finance directly the psychotomimetic drug program now supported by reimbursement from the Department of Defense. The Institute has a direct interest in this research program and believes that it should properly be supported through the NIMH appropriation.

During 1961 the Institute initiated a small research program in neurobiology. It is evident that this is a highly important area of research, which requires substantial strengthening and expansion. An increase of $150,000 and 15 positions is requested for this purpose.

Clinical Neuropharmacology Research Center, increase of $275,000.—Both storage and experimental facilities for animals at the Clinical Neuropharmacological Research Center are proving to be grossly inadequate. Professional estimates for the structural changes needed to provide necessary expansion have been obtained. The approximate cost will be $175,000. Rental of automatic data analysis equipment is needed for the speedy processing of polygraph data in studies of human psychophysiology. The rental cost of this equipment is estimated at $100,000 per year.

Review and approval of grants, increase of $668,000

An increase of 31 positions and $371,000 is requested for this function. Although the Institute's grants programs have grown in complexity and diversity over the past several years, the staff charged with the responsibility for directing and servicing these greatly expanded programs has not grown accordingly. The grant increases discussed in these estimates will increase the amount of staff work required in all areas (with particular emphasis on program analysis), and therefore will require an increase in staff.

An increase of $297,000 is requested for centrally furnished review and approval services.

Training activities, increase of $200,000

An increase of eight positions and $100,000 is requested for this activity. Institute staff must be maintained at the highest level of proficiency if they are to function effectively in the complex field of human behavior. In order to keep Institute personnel abreast of new knowledge, techniques, and methods that are constantly being developed, certain selected members will require additional training ranging from short refresher courses to longer periods of intensive study.

As the Institute has expanded its programs and moved into new areas of research, it has become more important to conduct activities of this nature. The $100,000 requested will make possible additional training of Institute personnel.

An increase of 12 positions and $100,000 is requested for the second phase of the career development program. This program is designed to provide a cadre of trained psychiatrists for the Public Health Service. It is currently proposed to initiate this program in 1961.

Professional and technical assistance, increase of $350, 000

Community services programs, increase of $200,000.—An increase of $200,000 is requested in order to establish a new demonstration, and strengthen the Mental Health Study Center.

The translation of research leads and findings into applicable, field-tested, practical methods and techniques in the field of community mental health has long been a responsibility of the Community Services Branch. The establishment of the Mental Health Study Center in Prince Georges County and its gradual development from a relatively simple demonstration of community clinic operations to a complex of interrelated demonstrations has resulted in the accumulation of significant knowledge of a substantive nature. An important byproduct has been the development of know-how in the area of design and administration of demonstrations. A recent development has been the initiation of a demonstration in the field of alcoholism. Similarly, current demonstrations in school mental health and drug addiction have already added to our knowledge on the applicability of new techniques in these areas.

The success of these demonstrations is evidenced by the large number of inquiries about them, the visits to them by professionals, and the adoption by communities of many of the demonstrated practices. The repeated requests from the States for more demonstrations has reinforced the need for enlarging this successfully operating program area.

The Institute proposes expansion along three dimensions, operationally, categorically, and geographically. Operationally, the need is for the demonstration of simple, practical, case findings, case holding, and case handling techniques which do not involve the use of the relatively expensive interdisciplinary team. Categorically, the need is for demonstrable approaches in the field of aging, school mental health, mental retardation, juvenile delinquency, alcoholism, and rural mental health. Geographically, demonstrations should be established as broadly as possible. Also, demonstrations should be replicated with different population groups and in different types of communities.

To this end, we propose the establishment of a demonstration in school mental health, and expansion of the Mental Health Study Center.

Psychopharmacology service center, increase of $150,000.—Although the programs administered by the Psychopharmacology Service Center have increased dramatically since 1959, the Psychopharmacology Service Center's staff had no increase in that time. Therefore, a minimal increase of 15 positions and $150,000 is requested.

Administration, net change of $217,000

An increase of 22 positions and $217,000 is requested for this function. Within the past 4 years the Institute has achieved a position of primary responsibility for the support of research and training in the broad field of mental health. As its programs have grown both in size and complexity, it has become increasingly important that it be headed by a strong coordinating and directing group. This increase will make possible strengthening of program direction, planning, and administrative management activities.

NATIONAL HEART INSTITUTE

1962 estimates—Prepared on basis of professional judgment of Institute Director

Activities	*Total estimate*
Grants:	
Research grants	$88, 500, 000
Research fellowships	4, 100, 000
Training	14, 800, 000
State control programs	5, 000, 000
Total grants	112, 400, 000
Direct operations:	
Research	11, 400, 000
Review and approval of grants	1, 826, 000
Training activities	300, 000
Professional and technical assistance	15, 540, 000
Administration	400, 000
Total direct operations	29, 466, 000
Total estimate	141, 866, 000

EXPLANATION OF INCREASES

Research grants, increase of $22,313,000

This amount includes an increase of $3 million over the funds included in the 1962 revised estimate for new grants and carryover of grants approved but unpaid in 1961. This increase will provide for support of additional worthwhile projects anticipated in areas of special interest in cardiovascular research.

An additional amount of $3,188,000 will permit the expansion of the program of institutional research grants to 10 percent of the total amounts provided for research grants. The revised estimate for 1962 applied 5 percent of amounts provided for research grants to the institutional grants.

An increase of $8 million is included to supplement funds ($7 million) available to establish and maintain cardiovascular clinical research centers during the coming year. This estimate is based on response to the program to date which has indicated strong interest in centers for clinical research in cardiovascular problems.

An increase of $7 million over the amount ($7 million) provided in the 1962 revised estimate is included to accelerate and expand the program of primate research centers. This amount would be used during the next year to meet the expressed need and interest for additional primate research centers.

The final segment of the increase, $1,125,000, is an estimate of the additional funds which could be used effectively in international research in cardiovascular fields.

Research fellowships, increase of $1 million

The increase in the fellowship program would provide for approximately the following additional awards: 35 postdoctoral fellows, 10 special fellows, 7 senior fellows, 9 career professorships, and 25 special fellowship grants. The increase would raise the total number of fellowships to be supported in 1962 from 434 to about 520.

Special fellowship grants, a program not previously described under this appropriation, will support promising young investigators in the cardiovascular field who are not yet eligible for awards at a higher level and supply important additions to the teaching and research staffs of sponsoring institutions.

Training grants, increase of $5,196,000

The increase in training grant funds would be utilized in the graduate training program to expand cardiovascular training activities in areas of current need in both research and clinical fields. Recent research progress has opened new lines for investigation and pointed up serious shortages in trained personnel. The areas in which increased training would be supported are:

Cardiovascular lipid research.—Three major areas in cardiovascular lipid research in which special needs exist for more trained researchers are: (1) newer methods of lipid analysis; (2) biochemical and nutritional aspects of atherosclerosis; and (3) investigative studies on the relationship of hormones to lipid metabolism.

Cardiovascular therapeutic evaluation.—Few medical schools have full-time clinical investigative pharmacologists in the clinical departments. Since as many as 400 new agents of biological activity are developed each year by the pharmaceutical industries, an acute need exists for trained clinical pharmacologists.

Experimental cardiovascular radiology.—Investigators trained in specialized techniques in radiology, such as angiography, cardiography, and radioisotopes, are urgently needed.

Cardiovascular immunology.—With the rapid advance of surgical techniques related to the transplantation of organs, training in the field of tissue immunology has become of major importance.

Cardiopulmonary research.—Training to produce the cardiovascular pulmonary physiologists needed in this research area involves modern techniques of clinical cardiovascular evaluation, as well as advanced training in mathematics, physics, physical chemistry, and statistics.

Cardio-renal research.—Research training programs in cardiorenal disease provide training in the investigation of the problems of serotonin metabolism, renal tissue enzymes, and effects of endocrine control of water and electrolyte metabolism.

Cardiovascular physiological research.—Training in these fields is designed to cover a range from electrophysiology of cardiac muscle and basic cardiodynamics to long-term clinical studies.

Cardiovascular hematology.—Knowledge of coagulation and thrombolysis has become an increasingly important area, with possible widespread clinical application. Training in diagnostic techniques utilizing radioactive isotopes and chemotherapeutic agents is needed.

Cardiovascular surgery.—Training to improve the total understanding of the physiologic, pathologic, diagnostic and therapeutic approach to the cardiovascular disease amenable to surgical treatment is important to the research effort.

Cardiovascular embryology, development, and genetics.—Expanded training is needed in these fields concerned with the occurrence of congenital heart disease.

Cardiovascular medical instrumentation.—Training programs utilizing the interdisciplinary approach, combining physical and biological sciences, can produce scientists to advance the field of medical instrumentation.

Pediatric cardiology.—Training in this area offers the skills necessary for conducting research in the fundamentals of cardiovascular problems in children.

State control programs, increase of $1,500,000

Each dollar placed in this formula elicits a matching dollar from the States which is used directly for prevention and control of heart diseases. States must have programs commensurate with the large body of knowledge and new concepts as they become available. Activities in the control of hypertension and congestive heart failure, and of instrumentation techniques, cannot be added to State programs without additional facilities. The proposed increase will have an impetus several times its size in helping the States to expand into modern control areas.

Research, increase of $1,500,000

This budget proposes an increase of $1,500,000 over the 1962 revised estimates. Two-thirds of amount, $1 million, is proposed for the development and support of decentralized heart research in PHS hospitals. Initiation of this program involves the conversion to laboratory usage of roughly 5,000 square feet at each of three locations, at a cost of $35 the square foot. This would be a nonrecurring cost approximating half of a million dollars. The estimated cost of carrying on this decentralized program in subsequent years would approximate a half a million per year.

The final third of the increase would provide for reorganization and strengthening of programs in epidemiology, biometry, and geographic pathology. This would include expansion of research studies and would provide staff consultation and site inspection of programs in international medical research and training.

Review and approval of grants, increase of $337,000

This increase is related to the expanded grants programs. Provision is made for additional staff, for expenses of the Council and Training Review Committee, and for activities connected with review and approval of grants for international medical research.

Training activities, increase of $114,000

This amount would provide for specialized training of PHS personnel to meet particular program needs, and for the support of additional administrative interns.

Professional and technical assistance, increase of $12,740,000

The increase includes $12 million which would be used to plan and initiate a program of homemaker and home nursing services. Care of sick and disabled heart patients at home through these plans would reduce the need for institutional care and reach an estimated million cardiovascular disease patients a year who otherwise would receive neither hospital nor adequate home care.

A high percentage of the victims of cardiovascular diseases (stroke, heart failure, and the like) need help to prevent disintegration of their homes during the period of their illness. A large number of States have recently, in studies and reports made for the White House Conference on Aging, made clear their recognition of these needs and their desire to meet these needs through homemaker and home nursing services.

Homemaker service is home help service to cardiac patients who are convalascent, aged, acutely or chronically ill, through employment of "homemakers," mature, specially trained women with skills in homemaking, who can help maintain and preserve family life that is threatened by illness, death or other problems.

Home nursing service is nursing care of these sick persons at home by nurses specially trained in problems of cardiovascular disease.

The first year of this program would be devoted to planning and initiating a comprehensive program, with $6 million devoted to the homemaker and $6 million to the home nursing services. Existing knowledge would be organized and training programs developed in the States in a coordinated program; trained personnel would be used in turn to train others. The contract mechanism would be used extensively to implement programs, using experience gained in limited programs already in existence in several States to expedite the new programs.

An increase of $220,000 is included to expand comprehensive stroke programs to a number of new communities, to capitalize upon the savings in medical care costs and reductions in human suffering which these projects can create.

The balance of the increase, $520,000, would implement expansion of services to patients with hypertension or congestive heart failure, who can benefit so greatly from community services such as nursing, nutrition, medical, and social.

Administration, increase of $93,000

This increase would provide for additional persons on the staff of the Institute Director, urgently needed to cover: (*a*) Support of the Director's Office as provided for in the reorganization plan; (*b*) implementation of program planning functions; (*c*) strengthening of the budget staff.

Construction grant for gerontology (nonmatching)	$12,000,000

A construction grant without a requirement for matching funds is believed to be the most practical method of financing a collaborative Aging Research Center bulding on the grounds of the Baltimore City Hospital. Unique opportunities for a broad, multidisciplinary attack on the biological, medical, psychological, and social and environmental aspects of aging are available here.

Architect's plans for the Research Center building have been developed by the Baltimore City Hospitals. The building would be eight stories high with a center core and two wings, situated on the grounds of the Baltimore City Hospitals. The building would house the Gerontology Laboratory of the National Heart Institute, now located in Baltimore City Hospital space, and basic science laboratories which constitute the ongoing research activities of the various departments of the Baltimore City Hospitals.

The proposal to establish the Aging Research Center at this location has the approval of the city of Baltimore.

NATIONAL INSTITUTE OF DENTAL RESEARCH

March 21, 1961 (Rev. 3-30-61)

1962 professional judgment budget

Activities	*Total estimate*
Grants:	
Research	$7,245
Fellowships	1,300
Training	5,500
Total grants	14,045
Direct operations:	
Research	2,706
Review and approval of grants	363
Administration	160
Total direct operations	3,229
Total estimate	17,274

GRANTS

Research projects, increase of $527,000 over 1962 revised estimates

The increase would provide for payment of full indirect costs on research grants.

Fellowships, increase of $540,000 over 1962 revised estimates

Of the increase requested, $50,000 will be used to expand the predoctoral fellowship program to encourage scientists to enter the field of dental research; $200,000 to expand the postdoctoral program since experience has demonstrated that more and more of the student part-time fellows are applying for postdoctoral support following graduation; $90,000 to expand the special fellowship program in such areas as congenital anomalies, electromyography, periodontal disease, radiation, and electron microscopy; $100,000 will be used for the special fellowship grant program which was initiated in October 1960 to provide advanced or specialized training for young investigators not yet eligible for an award at a higher level to assist in the development of a research and academic career; and $100,000 for the regular senior fellowship program to encourage and support the more advanced professional personnel in academic and research careers.

Training, increase of $2,209,000 over 1962 revised estimates

Of the increase, $1,300,000 would be used for expansion of the chairside assistants program which was initiated in 1961. This would permit the awarding of supplementary grants to those schools which have larger program demands due to larger class enrollments.

Of the balance, $545,000 will be used for expansion of support at graduate training centers which have demonstrated their ability to operate on a highly productive basis and have indicated that facilities are available, and $364,000 will be used to support training in especially critical areas such as (1) hospitals where academically oriented dentists would be training in several clinical specialties for clinical teaching and research in dental schools, (2) schools of public health to train dentists in epidemiology and related fields, and (3) periodontal research and cleft-palate investigations in large dental clinics and in schools presently without training programs.

DIRECT OPERATIONS

Research

No change from 1962 revised estimates.

Review and approval of grants, increase of $53,000 over 1962 revised estimates

This increase will provide the additional staff and other objects necessary for review and evaluation of applications and for processing grants in connection with the expanded research grants and training operation.

Administration—Increase of $12,000 over the 1962 revised estimates

This increase in administration will cover additional administrative responsibilities connected with the expanded program.

ARTHRITIS AND METABOLIC DISEASE ACTIVITIES

1962 estimates prepared on basis of professional judgment of Institute Director

Activities	*Total estimate*
Grants:	
Research	$61,000,000
Fellowships	2,500,000
Training	14,060,000
Total grants	77,560,000
Direct operations:	
Research	10,868,000
Review and approval of grants	1,407,000
Administration	325,000
Total direct operations	12,600,000
Total	90,160,000

RESEARCH PROJECTS

Research grant applications reflect a solid continuation and expansion of the highly important and productive component of basic research as well as introducing the desirability and necessity for expanded support in various aspects of clinical investigation. The constant accelerated increase in numbers of applications which have been assigned to this Institute for review and support now reflects these twin emphases. Receipt of applications is currently running about 40 percent higher than at the same time 1 year ago. Furthermore, it can be confidently predicted that, in a well-balanced program of the type which the Institute should support, this rate of increase both in number of applications and in funds requested will continue. A heartening corollary of this observation is the fact that, while the applications awarded in the basic areas continue to be of uniformly high quality, there has been a marked increase in the quality of proposals submitted in the very recent past for financing projects in clinical research.

The increasingly difficult task of bridging the gap between the growing body of pertinent information derived from studies on fundamental problems and its application in the cure and prevention of disease is of great importance. At the same time it is essential to continue to provide for all possible worthy research projects in fundamental problems in order to pursue promising leads uncovered in the laboratory.

Funds are also included in this estimate for the establishment of additional multicategorical clinical research centers. The opportunity for the physiologist, the pathologist, and the biochemist, as well as the clinician, to truly and effectively relate their investigations and information in a well coordinated approach to a given problem holds great promise for the type of balanced, timely progress most desirable in medical research. It is this approach that most ideally bridges the gap between discovery and application.

It is expected that deserving grant applications in the magnitude indicated herein will be received during 1962, and with the increase proposed, this Institute will be able to efficiently administer such a program.

Fellowships

Funds requested in the fellowships area reflect a growing interest in training for basic research and clinical investigation in problems relating to arthritis, diabetes, gastroenterology, and general metabolism. During fiscal years 1960 and 1961 there has been a significant increase in numbers of applications in those fields, and it has not been possible to support many well-qualified individuals. A backlog of approximately $1 million is currently in hand.

The new program for senior career development is particularly pertinent and will augment and bring further depth to the broad areas of interest and responsibilities of the Institute.

Training

The increase indicated in funds for graduate training grants is based on an estimate of the manpower needed for development of programs for academic medicine, including clinical research, in medical schools currently not engaged in or not adequately staffed for these purposes. Such programs in this estimate include not only the traditional five major areas of support (arthritis, diabetes, gastroenterology, hematology, and general metabolism), but also provide for support in the new areas of dermatology, orthopedics, and nutrition.

It is considered essential that the requested expansion in this activity take place as soon as possible to meet requirements for the adequate staffing of present research and teaching facilities, and to provide a nucleus of trained manpower for the many proposed new medical schools and other expansions of teaching facilities.

DIRECT OPERATIONS

Research

Included in this activity—in addition to fundamental laboratory studies and an extensive clinical investigations program—are international studies in civilian nutrition conducted throughout the world in collaboration with the Interdepartmental Committee on Nutrition for National Defense, and collaborative epidemiologic, biomathematical, and genetic programs conducted by the Institute's Epidemiology and Biometry Branch. In this presentation, reflecting the professional judgment of the Institute Director, the following brief explanation of the net change is described; $150,000 is requested to support expanded programs in international civilian nutrition studies in selected countries throughout the world; 3 positions and $150,000 is required to strengthen out the epidemiology and biometry staff and provide sufficient funds for contracts with cooperating universities in the United States and abroad and for mobile epidemiologic field studies—including the purchase of a mobile van or trailer; 22 positions and $427,000 for required additional staff and necessary equipment to support studies conducted by senior investigators in the field of molecular biology, nutrition research, enzymes and cellular biochemistry, physical biochemistry, physiology, metabolic enzymes, clinical hematology, gastroenterology and clinical diabetes studies. The total also includes funds to purchase computer time for research in computer technology as applied to biology and for the purchase of specialized items of equipment and the replacement of obsolete scientific equipment. Included, also, is $426,000 for research services furnished centrally.

Review and approval

One hundred and fifty-eight thousand dollars and 12 additional professional and clerical personnel are provided to administer the proposed expanded grants programs. This includes funds for initial equipment requirements, travel, printing and publication, communications and other miscellaneous expenses. Further provided is $199,000 for services furnished centrally.

Administration

The increase provided for this activity is for three positions and $60,000 to furnish staff assistants to the Institute Director for special program analysis and review activities and for the planning and preparation of a projected series of special and continuing reports covering all Institute programs. Also included is $29,000 for services furnished centrally.

Allergy and Infectious Disease Activities, Mar. 21, 1961

1962 estimates prepared on basis of Institute Director's professional judgment

Activities	*Total estimate*
Grants:	
Research	$43, 167, 000
Fellowships	2, 933, 000
Training	8, 383, 000
Total grants	54, 483, 000
Direct operations:	
Research	9, 618, 000
Review and approval of grants	982, 000
Administration	277, 000
Total direct operations	10, 877, 000
Total estimate	65, 360, 000

INTRODUCTION

It is the opinion of the Director, National Institute of Allergy and Infectious Diseases, that the proposed increase recommended in the grants and direct operating areas of the Institute are feasible in terms of present resources and interests.

Because of the mutability of the Institute programs, needs must be anticipated and funds made available to continue and expand present programs, and to prepare the way for new programs evolving out of present studies.

Research grants

1962 revised estimate	$31, 637, 000
1962 professional judgment	43, 167, 000
Increase	11, 530, 000

Respiratory viruses.—During the past year a committee of experts has been developing a program which is designed to provide type-specific antigens and antisera for the characterization of viruses which are responsible for respiratory infections. The initial stage of the program envisions the preparation of specific biologicals for the adenoviruses and will provide an opportunity for identification and accurate classification of the first 18 human adenovirus strains. Eight additional human strains and 10 animal strains require developmental research before production of specific reagents may be undertaken. Twenty-four additional respiratory viruses, including such agents as smallpox, measles, myxoviruses, mumps, etc. also require type-specific sera and antigens for the use of investigators working on these problems. The program to provide these necessary research and diagnostic materials will require approximately $2 million.

Influenza.—During the past 2 years the National Advisory Allergy and Infectious Diseases Council has supported a program which is designed to prevent the waning of interest in support of influenza research through a special committee charged with identifying research needs in this particular epidemic disease. For the fiscal year 1962, $200,000 has been proposed for the support of these special research projects. In addition to the work on specific research activities, the investigators receiving support agree to hold themselves in readiness to study any unusual incidence of influenza or acute upper respiratory disease which occurs in their environs. The support of this program will insure a group of highly skilled investigators capable of being immediately mobilized for study in the event of influenza epidemic.

Urinary tract infections.—In the past 2 years the problems of infection in the urinary tract, with both bacterial and viral agents, has been the subject of increasing interest and research. Results to date are more encouraging and have pointed out the ability of investigators to isolate infectious agents at very early stages of tissue invasion in the urinary tract. Additional support for research in this area may well provide answers to many of the perplexing problems presently causing such widespread disease and disability from chronic kidney pathology and urinary tract infection. It is estimated that approximately $1 million would be required to fully initiate this program.

Enteroviruses.—Although these viruses have long been recognized as one of the primary causes of acute gastrointestinal disease, understanding of their mode of action and exact classification and characterization of their infectious process is little understood. With the advent of a program which will provide specific biological reagents more sophisticated investigations may be undertaken and the exact nature of morbidity created by these agents identified. It would be expected that approximately $1 million would be required to support this program.

Normal program expansion.—During the past several years there has been a consistent rate of increase in the applications for research which have been received by the Institute. This has, in general, approximated 20 percent above the preceding year. Recognizing that it is not expected that the rate of approvals in new applications is as high as applications received from more experienced investigators, the remainder of the funds proposed should be held for the support of proposals which it is anticipated will be received from worthy investigators who are recommended for approval.

	1962 revised estimate	1962 professional judgment	Increase or decrease
Research:			
Continuations	$20,512,000	$21,980,000	$1,468,000
Supplementals	1,961,000	2,088,000	127,000
New grants:			
Carryover	1,285,000	1,285,000	0
Wholly new	4,899,000	12,764,000	7,865,000
Institutional research grants	1,520,000	3,000,000	1,480,000
Increase Government share of full indirect cost of grants awarded on or after Jan. 1, 1962	210,000	0	−210,000
Subtotal, regular program	30,387,000	41,117,000	10,730,000
Special programs:			
International medical research	500,000	1,300,000	800,000
Gorgas Memorial Laboratory	250,000	250,000	0
Categorical research centers	500,000	500,000	0
Subtotal, special programs	1,250,000	2,050,000	800,000
Total research grants	31,637,000	43,167,000	11,530,000

Fellowships

1962 revised estimates	$1,400,000
1962 professional judgment	2,933,000
Increase	1,533,000

Additional funds would provide increases in all areas of currently supported fellowship awards. Support of these awards is imperative if adequate training of scientists with specialized skills is to be accomplished. Greater numbers of these specifically trained scientists are needed in order that the research endeavors in the fields of allergy and infectious diseases may continue at the present rate.

Projection table

	1962 revised estimates	1962 professional judgment	Increase
Postdoctoral	$760,000	$1,059,000	$299,000
Special awards	340,000	671,000	331,000
Senior grants	100,000	345,000	245,000
Career professorships	200,000	858,000	658,000
Total	1,400,000	2,933,000	1,533,000

Training

1962 revised estimates	$5,290,000
1962 professional judgment	8,383,000
Increase	3,093,000

The Institute training grant program is now in its third year of operation. The specially trained scientists under this program are beginning to assume academic positions in the fields of allergy and immunology, tropical medicine and parasitology. But, an increasing number of young investigators must be adequately oriented in these areas if the Nation is going to continue in its efforts to eliminate and/or prevent these allergic and infectious diseases. Many highly specialized individuals are desperately needed to fill the faculty vacancies in our medical schools. A number of these training grants are in an area where opportunities for research training have been woefully inadequate.

Direct research

1962 revised estimate	$8,978,000
1962 professional judgment	9,618,000
Increase	640,000

It is frequently difficult and sometimes impossible to anticipate the opportunities for important advancement in answering problems of medical research. A new discovery or refinement of techniques or equipment may encourage scientists to undertake an approach to a problem that may offer new hope of solution. The two research projects of first importance described below come within this category:

Virus respiratory disease studies—11 positions and $256,000

Respiratory tract illnesses represent the most common form of human infectious disease. Twenty million febrile illnesses are estimated to occur in preschool age children each year. Fifty to sixty thousand deaths are attributed to pneumonia and other forms of respiratory diseases, far exceeding the public health importance of poliomyelitis in terms of mortality. Current statistics suggest an upper trend in fatal respiratory illnesses.

During the past 9 years, advances in laboratory methods, notably tissue culture and fluorescent antibody techniques, have resulted in the recognition of at least 96 new viruses, of which 20 cause human respiratory disease. Approximately 60 percent of hospitalizing respiratory diseases in children can now be identified. A recently described virus, the respiratory syncytial virus, accounts for 20 percent, the parainfluenza virus 15 percent, adenovirus 10 percent, Eaton agent 10 percent, and influenza 5 percent. Methods now appear to be on hand to close the gap by identifying the cause of the remaining 40 percent of children's infections and the even greater challenge of adult respiratory disease. Facilities for prisoner-volunteer studies have been developed which can rapidly answer many of the critical questions. More is needed to be learned of the natural history of the infections, including the immunity and therapy. Development of vaccines awaits more detailed knowledge of the biology of the viruses and methods of production. Live virus vaccines need to be explored since they give promise in the long run of the most effective control procedure. The promising results of live polio vaccine demand an increasing tempo of research in this area.

It is proposed to expand the current studies in the Laboratory of Infectious Diseases to meet these urgent and challenging problems. Eleven new positions and adequate funds to purchase antigens and antisera, tissue culture, and laboratory animals are necessary.

Collaborative studies of viruses and cancer—18 positions and $384,000

Reliable and ready laboratory tools to demonstrate tumor viruses are now available by applying those techniques used in general virology. Tissue culture methods and specially defined animal lines have opened new avenues for understanding the role of viruses as a cause of tumors. Greater knowledge of the natural history of these processes is required immediately. Better definition of latent virus infection in animals, better animal research facilities, more refined diagnostic tools, and opportunities for field studies in both human and animal cancer are essential to the advancement of this problem.

The Laboratory of Infectious Diseases has probably the greatest efficiency for studying the wide range of viruses in animals and man of any single laboratory anywhere in the world. Complex problems require large resources for their solution.

In conjunction with the National Cancer Institute it would be possible to study animal and human cancer in natural environments under the NCI Washington County environmental study program. Here facilities are available for field observations of the disease in both urban and rural environments. Such an effort in unique in concept, resources, and opportunities. Specifically, this includes the completion of a natural history study of polyoma and other mouse tumor viruses in Washington County, a seroepidemiologic study of human cancer for detecting virus infection encompassing over 100 viruses, correlation of information on environment such as background radiation, special study of chicken tumors using new tissue culture techniques, and a study of viruses associated with lymphoma in cattle.

Requirements are a base virus laboratory closely identified with the Laboratory of Infectious Diseases, a serologic study group, a field laboratory located in Hagerstown, and an epidemiology team located in Hagestown.

Review and approval

1962 revised estimate	$773, 000
1962 professional judgment	982, 000
Increase	209, 000

Additional funds would provide $209,000 for payment to the National Institutes of Health management fund which represents the proportionate share of costs for services provided centrally.

Administration

1962 revised estimate	$244, 000
1962 professional judgment	277, 000
Increase	33, 000

If additional funds were made available, they would be used to support eight new positions in this activity. These funds would recognize the need for additional staff necessary to deal with the increased research activities. new programs, and administrative complexities of the Institute.

CONSTRUCTION REQUEST BASED ON INSTITUTE DIRECTOR'S PROFESSIONAL JUDGMENT

March 21, 1961

ROCKY MOUNTAIN LABORATORY

During the past 15 years the Rocky Mountain Laboratory has evolved from a research activity concerned with a few important arthropod-and-insect-borne diseases to a well integrated and extremely productive facility encompassing a broad spectrum of medical research. While the staff of the Laboratory has increased during this time from less than 100 employees to more than 150, the overall size of the Laboratory has remained essentially static with the exception of an inexpensive animal building built last year. To accommodate the increased staff and the changing equipment and service needs of new programs, it has been necessary to resort to conversion and reutilization of space and adjustments and modifications that have accumulated a number of problems related to the heating, ventilating, electrical and related services of the plant. A careful study of existing problems reveals several areas of obsolescence and serious inadequacy which if corrected will greatly increase the productivity. safety and efficiency of the Laboratory:

(*a*) Correction of deficiencies in the heating plant to provide better ventilation and humidity, safer and more uniform temperature control of lab and animal rooms, to reduce health hazards, to replace obsolete air filter equipment, and to extend filtered air to certain areas. Replacement of chemically corroded ducts, central panel control for the powerplant, miscellaneous plumbing. electrical and waste disposal improvements and replacements	$200, 000

(*b*) To install glasswashing equipment needed to meet the demand for more sterile glassware. To install a modern central animal cage washer and a steam sterilizer of wastecans used for contagious agents	$25, 000
(*c*) The medical library for the Rocky Mountain Laboratory has now outgrown its space and, being on the third floor of a building not designed for the weight, presents a space problem and a safety hazard that needs attention. To move the library to ground floor space now used for the garage and shops, to construct a single story cement slab, cinder block structure to house the garage and shops, and related costs	170, 000
(*d*) Construction of facilities in which to conduct exacting research requiring strict isolation of pathogenic agents, to prevent cross contamination, and to reduce the hazard of laboratory-acquired disease. (A recent outbreak of Q fever that required closing the laboratory to visitors for several months emphasizes the pressing need for a lab physically separate from other buildings where highly infectious agents can be studied without exposing other workers and visitors to undue hazard.) Such facilities could be provided at a minimum cost by using the basic building plan of the recently built animal production building; a simple single story, cement slab, tile, and concrete block structure. This building can be built and outfitted for laboratory and infectious animal use for approximately	255, 000
Total	650, 000

NEUROLOGY AND BLINDNESS ACTIVITIES

March 21, 1961

1962 estimates prepared on basis of professional judgment of NINDB Institute Director

Activities	*Total estimate*
Grants:	
Research	$49, 400, 000
Fellowships	1, 500, 000
Training	9, 500, 000
Total grants	60, 400, 000
Direct operations:	
Research	9, 636, 000
Review and approval	1, 265, 000
Training	100, 000
Administration	365, 000
Total direct operations	11, 366, 000
Total estimate	71, 766, 000

GRANTS

Research grant program—increase, $14,016,000

For 1962, it is estimated that the continuation requirements and the normal growth of new approved applications will be approximately $35,800,000. This would support approximately 1,556 projects.

Estimated approved grants	$35, 800, 000
Following are special program areas of added particular concern:	
1. The development of a broad program for the testing of drugs, including those for epilepsy, Parkinsonism, myasthenia gravis, and disorders of vision, including uveitis and glaucoma	3, 000, 000
Projects with industry for the development of special instruments, and for the adaptation of industrial techniques to special problems in medical research. This will include such things as certain new computer techniques applicable to the study of neuropathological material, electronic devices for the study of nervous activity, and special devices for the testing of intraocular pressure for the removal of foreign bodies from the eye.	
Special studies of the infectious origin of neurological and sensory disorders. There is increasing evidence to suggest that certain chronic neurological disorders may be the result of viral or bacterial infection of the nervous system. The evidence suggests that viruses may remain latent within neural tissue over periods of many years leading to neurological symptoms only when intercurrent events reduce the resistance of the tissues, or slowly developing chronic effects eventually make their damage apparent. Newer techniques of isolation now provide the potential for an all-out effort to isolate organisms from conditions such as multiple sclerosis, certain forms of Parkinsonism and infantile epilepsy. Such an undertaking will be extremely difficult. It is unlikely that such viral agents will grow in lower animals—the isolation efforts should be carried forward with monkeys. The slowly deveolping nature of the illness indicates that rather long periods of observation of inoculated animals will be required. These programs will require the obtaining of animals with a relatively low level of previous infection, and a known degree of viral exposure and contamination, the inoculation of these animals with material from patients suffering from these diseases, and the provision of isolation units where these animals may be observed for varying periods of time free from incidental contamination.	
While many or most of these activities can be supported by grants, it is deemed desirable to have the authority to enter into contracts with research organizations when the studies can best be conducted by that type of arrangement.	
2. International cooperative research programs, including the special areas of cerebrovascular disease and perinatal studies, and the NIH central program in infectious disease studies ($369,000)	2, 000, 000
3. The development of special broad multidisciplinary research projects. This envisages the establishment of centers concentrating on multidisciplinary well-rounded programs for attack against multiple sclerosis, amyotrophic lateral sclerosis, disturbances of vision, disturbances of speech and hearing, epilepsy, Parkinsonism, and diseases of muscle; and the establishment of special facilities in neurochemistry and neuropathology as facilities to be called upon by several institutions, and to serve as regional resources	5, 000, 000
4. Institutional grants (10 percent of normal program.)	3, 600, 000
Total research projects	49, 400, 000

Research fellowships—increase, $520,000

Applications for fellowships have increased in the fields of neurological and sensory disorders. This increase will support a total program of 139 awards costing $1,500,000 as against 112 awards and $980,000 in 1961.

	1961		1962	
	Number	Amount	Number	Amount
Postdoctorate	89	$580,000	89	$580,000
Senior	8	100,000	26	320,000
Career professorship	15	300,000	24	600,000
Total	112	980,000	139	1,500,000

Training grants—increase $1,654,000

Graduate Training, increase $1,654,000.—The unusual need for trained investigators in the area of neurology, sensory disorders, and related disciplines makes it imperative for the Institute to continue to advance its training program as rapidly as possible.

The Institute's training program has been in effect for 8 years and is now well established. During 1961, there will be approximately 187 training programs providing training for 729 trainees.

Training is already well developed in clinical neurology with 65 programs and approximately 235 trainees, and in ophthalmology with 33 programs and 214 trainees. No major expansion is contemplated in these two areas. Clinical otolaryngology and medical audiology training have not advanced as rapidly as these other programs and have been expanded to approximately 27 programs with 150 trainees in 1961. These programs need further strengthening by placing greater emphasis on the applicability of basic research methods to clinical problems. Pediatric neurology training has been initiated in the last 2 years; 10 programs and 31 trainees are being supported. There is a need for more scientists with knowledge of basic research techniques who have the ability to apply these talents to the problems of neurological and sensory disease.

It is estimated that an additional 47 new programs, chiefly in the basic sciences and pediatric neurology will be needed in fiscal 1962 if we are to provide for our future manpower needs.

1962 projection

1. Continuation of 1961 program (at 90 percent)	5,500,000
2. New normal growth	2,000,000
Subtotal	7,500,000
Direct traineeships, increase 0. In 1962, this program will support 230 trainees	2,000,000
Total training	9,500,000

DIRECT OPERATIONS

Research—Increase $1,300,000

Collaborative and Field Research, increase $500,000.—$500,000 and 57 positions would be used to strengthen the Institute's program in collaborative research.

At the present time, the major emphasis in this area of research is the collaborative project in cerebral palsy, mental retardation, and other neurological disorders of childhood. The project recently completed its second year of operation, after 2½ years of intensive preparation. About 5,500 expectant mothers and 4,500 babies were studied in the pretest phase, and as of December 31, 1960, approximately 13,500 expectant mothers and 8,000 babies had been enrolled in the main phase of the project.

The project will eventually involve some 50,000 expectant mothers and their children from all parts of the Nation. Record keeping begins in early pregnancy and continues through labor and delivery into the early years of the lives of the children.

Working on the project, with research grants at 15 private medical institutions across the country, are obstetricians, pediatricians, neurologists, and specialists in a least a dozen other medical and related scientific fields. All of them have a common goal: to gain new knowledge about the relationship between events and circumstances of pregnancy, labor, delivery, and the first month of life on the one hand, and the later occurrence of neurological or sensory disorders on the other. Their common hope is that this new knowledge will make it possible to prevent these disorders and thereby enable every child to lead a full and useful life.

Recent developments of the protect include the revision of examination forms and manuals to further assure uniform collection of data on study mothers and babies; the development and adoption of methods for post-mortem examination of all abortions, stillbirths, and children dying in the first month of life; and the final preparation for the routine screening to begin in 1961 of blood samples from study mothers during pregnancy for evidence of virus infections.

In addition to strengthening the collaborative project in the study of perinatal factors, some of this increase would be used for staff and their support in separate epidemiological, biometric, international, and geographic pathology studies, such as amyotrophic lateral sclerosis in Guam, "Kuru" in New Guinea, and the prevalence and incidence of neurological disorders, with increased emphasis on Parkinsonism, cerebral arteriosclerosis and stroke, and the demyelinating diseases.

Puerto Rico projects, increase $800,000.—In addition to and paralleling the collaborative project in perinatal studies, the Institute has an active program of laboratory research relating to mental retardation and other neurological and sensory disorders of infancy and childhood. This direct research program is underway at the Bethesda laboratories and in Puerto Rico.

The Institute's Laboratory of Perinatal Physiology in Puerto Rico, in collaboration with the School of Medicine of the University of Puerto Rico, was established specifically to study perinatal factors leading to cerebral palsy and other neurological defects, and to observe under laboratory conditions the development of the nervous system of both normal and defective animals.

The initial objective to ascertain the role of asphyxiation in producing neurological disorders is being approached. Infant monkeys asphyxiated and resuscitated at birth have been found to develop all degrees of neuromotor and psychological handicaps, including syndromes resembling cerebral palsy, epilepsy, deafness, and mental retardation.

Recent investigations have included the study of the pattern of pathological changes demonstrable in the brains of asphyxiated monkeys. Behavorial tests have revealed abnormalities in normal-appearing monkeys deprived of oxygen at birth, and considerable information on normal physiological values in these monkeys has been collected and analyzed in preparation for further investigations.

New objectives of this laboratory are to standardize the physiological conditions during asphyxia and to measure damage under agreed criteria, and then to seek means of preventing nervous system damage by introducing certain therapeutic measures.

In addition, research activities with the free-ranging monkey colony on Cayo Santiago continue productively, and will be supplemented by other colonies on available islands.

Plans for the Laboratory of Perinatal Physiology are in process of reformulation. One basic principle is to provide facilities and resources both for full-time scientific staff and a changing group of visiting scientists of kindred interests in other institutions, so that this facility can serve as a center for perinatal research on primates. Initial productive contacts with outstanding investigators in Latin America have already been established.

Our initial experience with this project has been so successful that we now recommend an increase in the laboratory facilities in Puerto Rico, and request an appropriation of $800,000 to add approximately 12,000 net square feet of laboratory space. This request is further justified in an attachment.

Review and approval of grants, increase $84,000

Of this increase, $69,000 will support seven additional positions required for the processing, analyzing, and management of the grants and awards program. The remaining increase of $15,000 is for centrally furnished review and approval services.

Training activities, increase $50,000

This increase will provide training for five additional positions in universities and other appropriate institutions in order to supplement already acquired experience and academic training where special needs exist in the total neurology research program.

Administration, increase $42,000

This increase will support five additional positions required for clerical and technical assistance for administrative services on a centralized basis.

PROPOSAL FOR EXPANSION OF THE NINDB LABORATORY OF PERINATAL PHYSIOLOGY, SAN JUAN, P.R., INCLUDING CONSTRUCTION

March 30, 1961

It is estimated that $800,000 is necessary in fiscal 1962 to construct an additional laboratory facility for the project in Puerto Rico.

The availability, in 1956, of a free-ranging colony of rhesus monkeys, the only one of its kind in the New World, provided a unique opportunity for the prosecution of the experimental phase of the NINDB collaborative project in cerebral palsy and mental retardation. This was aided by the willingness of the School of Medicine of the University of Puerto Rico to collaborate in the project and to allow the NINDB to erect and furnish with suitable equipment a laboratory in neonatal newborn physiology.

The project was initiated by a contractual agreement between the NINDB and the University of Puerto Rico on April 16, 1956. Actual experiments on monkeys began in February 1957. There are now 35 employees on the project: the current budget (fiscal year 1961) is $310,000. Laboratory space, both at the School of Medicine of the University of Puerto Rico, at the outpatient clinic in San Juan, and NIH, totals approximately 9,000 square feet.

The free-range monkey colony on Cayo Santiago was purchased. The island contains about 37 acres and is leased from the University of Puerto Rico. The colony of Macaca mulatta monkeys, the only free-ranging group in the New World, was established on Cayo Santiago in 1938. The animals were brought from several regions in India and interbreeding has resulted in the development of a strong, disease-free, strain of monkeys. The colony was said to number nearly 500 animals in 1946, but because of excessive removal of animals, only about 120 remained when the project was taken over by the Institute on April 16, 1956. At the present time the colony numbers approximately 325 animals. Five feeding stations are now maintained on the island. There is a central laboratory, comprising approximately 1,500 square feet, furnished with refrigeration, operating room and X-ray equipment. This laboratory is being utilized for developmental studies and anthropometric investigation of the free-range colony.

The main function of the Laboratory of Perinatal Physiology is to conduct fundamental animal research on problems of development, growth and maturation, and the aberrations of these—particularly in respect to the nervous system—that result from introduction of adverse conditions during the prenatal, natal, and early postnatal periods of life. It is recognized, however, that its program will not be limited exclusively to this area of research. The principal experimental animal is the rhesus monkey.

The following considerations underlie the next recommended step: The project must develop within the orbit of the Medical Center of Puerto Rico and the University of Puerto Rico; both of these organizations are exhibiting substantial and healthy growth. The laboratory should ultimately become an integral component of the school of medicine of the university, and it should be staffed and operated largely by Puerto Rican scientists as the latter become available and interested. Therefore, it is recommended (A) that in the immediate recruitment of professional staff, primary consideration be given the available people in Puerto Rico who have the necessary qualifications and interest; and (B) that construction of an initial laboratory unit on the grounds of the medical center be started in close proximity to other neurological and research units.

For the time being, activities of the Laboratory of Perinatal Physiology should continue as a direct operation of NINDB, but a small committee of NINDB and the University of Puerto Rico administrators will be designated for the guidance of the program.

Research will be carried forward by competent scientists in the following disciplines: (*a*) morphology, including cytology, embryology and genetics; (*b*) fetal and gestational physiology; (*c*) psychology; (*d*) experimental neurology and electroencephalography; (*c*) neuropathology; (*f*) biochemistry, including neurochemistry; and (*g*) behavioral science and anthropology.

Each section head will be expected to develop research programs according to his competence and interests within the broader aims of the laboratory and NINDB. Each will advise the laboratory chief regarding needs of his section in respect to other professional and subprofessional personnel. However, it seems apparent that the initial number of professional positions required will be 16 or 17, with at least 9 or 10 now citizens of Puerto Rico. Of these, it is anticipated that 8 will be on duty June 30, 1961. More than 85 percent of all subprofessional and supporting staff are presently Puerto Ricans.

It is recommended that for the present the Laboratory of Perinatal Physiology continue to make full use of temporary space provided at the present medical school and at the USPHS Clinic, and at NIH in Bethesda. This temporary space comprises about 9,020 square feet and provides laboratories for nine professionals and housing for 250 monkeys.

New construction will be required in order to provide essential facilities for psychology, physiology, neuropathology, and biochemistry.

Therefore, it is recommended that an appropriation be sought for construction of the initial unit of the laboratory and animal colony building on the grounds of the Puerto Rican Medical Center. This unit should provide 52 modules for laboratories, for some central services such as cage washing and incineration, for offices, and for cage space for the animals undergoing study and experimentation.

On the availability of this new facility, there would be the following redistribution of modules between present and new space.

	Present	Revised space		
		In present space	Medical center	Total
Laboratories	18	10	24	34
Central services	6	6	8	14
Animal	14	22	20	42
Total modules	38	38	52	90
Total net square feet	[1] 9,020	[1] 9,020	[1] 12,480	[1] 21,600

[1] At 240 square feet per module.

For initial planning purposes, we estimate that the 12,480 net square feet in the new proposed building would convert to about 20,000 square feet gross space. Using a $40 cost per gross square foot, the estimated construction cost, including capital equipment, such as benches and hoods, would be about $800,000. Land will be furnished by the Medical Center.

In additon to initial construction costs above, scientific equipment and apparatus would cost approximately $513,000 for the new facility.

24 laboratory modules, at $12,000	$288, 000
8 central service modules, including incinerator and cage washer	75, 000
20 animal modules	125, 000
Miscellaneous	25, 000
Total	513, 000

Following is the estimated projected operating cost should the new facility be constructed:

	1961	1962 revised budget	Annual operating costs of expanded program
Positions	35	44	130
Space (net)	9,020	9,020	21,600
Cost	$310,000	$420,000	$978,000

We have used a 200 square foot per person figure to estimate total number of personnel; this is our average in research operations where many animals are involved. Also included are 10–12 employees to serve as truckdrivers, craftsmen, guards, cagewashers, and incinerator operators. Approximately 10 are also estimated for island operations.

Our current average employment costs are $5,300, due to lower salaries for laboratory animal caretakers and laborers ($1,976 per annum). We have also computed the costs of the expanded program on the 70–30 ratio of "Personal services" to "Other objects."

SUMMARY

In summary, the further development of the Laboratory of Perinatal Physiology should be carried forward in close geographical and administrative relationship to the University of Puerto Rico. The first step will involve the construction of a small building on the grounds of the medical center. This facility will comprise approximately 12,480 net square feet, and will provide laboratory space, certain central services, and housing for those animals undergoing active study and experimentation. It will include facilities for psychology, physiology, neuropathology, and biochemistry—disciplines which at this time appear to relate most directly to ongoing activities of present members of the faculty of the University of Puerto Rico. With the completion of this new building, the total operation will provide laboratory facilities for approximately 17 scientists, central services, and housing for up to 400 primates. Total estimated construction is about $800,000.

History of Budget Requests for 1962

Mr. Fogarty. So that we will have all these budgets in one place in the record, will you also prepare, in summary form, the complete history of the 1962 budget.

Dr. Shannon. Yes, sir.

(The data requested follows:)

National Institutes of Health

Development of 1962 budget estimates

[In thousands]

Obligations by Institute	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 President's original budget	Department of Health, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
General research and services	$138, 155	−$34, 123	$104, 032	−$8, 265	$95, 767	−$8, 363	$87, 404	$119, 275	$23. 934	$95, 341
National Cancer Institute	137, 035	−10, 003	127, 032	−13, 467	113, 565	−4, 273	109, 292	125, 672	8, 505	117, 167
Mental health activities	112, 185	−20, 518	91, 667	−1, 010	90, 657	−7, 735	82, 922	92, 182	3, 858	88, 324
National Heart Institute	124, 211	−7, 162	117, 049	−14, 794	102, 255	−10, 898	91, 357	105, 723	8, 650	97, 073
National Institute of Dental Research	17, 915	−992	16, 923	−2, 123	14, 800	−1, 765	13, 035	14, 631	748	13, 933
Arthritis and metabolic disease activities	85, 950	−13, 402	72, 548	−1, 736	70, 812	−8, 573	62, 239	73, 661	4, 921	68, 740
Allergy and infectious disease activities	64, 526	−12, 818	51, 708	−1, 645	50, 063	−5, 778	44, 285	52, 182	3, 860	48, 322
Neurology and blindness activities	71, 766	−14, 108	57, 658	−1, 513	56, 145	−6, 679	49, 466	57, 624	3, 524	54, 100
Total obligations	751, 743	−113, 126	638, 617	−44, 553	594, 064	−54, 064	540, 000	641, 000	58, 000	583, 000

ANALYSIS OF GRANT FUNDS 1961 AND 1962

Mr. FOGARTY. We will also place in the record your analysis of the adequacy of research grant funds for 1961 and 1962 which you prepared at our request.

(The tables referred to follow:)

National Institutes of Health

Analysis of 1961 research grants (reflects release of requested unprogramed reserves and release of IRG funds to support regular program)

	G.R. & S.	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Total
1. 1961 apportionment (excludes BOB reserve)	$41,844,000	$51,731,000	$31,455,000	$55,753,000	$5,777,000	$41,190,000	$28,370,000	$31,005,000	$287,125,000
(*a*) Actual transfer of funds through Mar. 31, 1961		−1,300,000	−3 0,000						−1,650,000
(*b*) Unprogramed reserves requested		1,196,800	1,820,000			674,500	714,300	559,700	4,965,300
(*c*) 1961 funds available for research grants	41,844,000	51,627,800	32,925,000	55,753,000	5,777,000	41,864,500	29,084,300	31,564,700	290,440,300
2. 1961 estimated continuation requirements	20,702,316	29,716,089	18,436,535	28,809,012	3,398,902	27,111,311	18,724,254	19,978,044	166,876,463
3. 1961 estimated supplemental requirements	1,418,582	1,512,398	794,735	2,928,967	127,725	1,913,837	1,894,855	1,764,262	12,355,361
4. 1961 estimated new grant approvals	17,175,545	7,421,967	10,660,350	11,593,410	1,735,373	10,607,054	7,633,241	7,258,933	74,085,873
5. Subtotal	39,296,443	38,650,454	29,891,620	43,331,389	5,262,000	39,632,202	28,252,350	29,001,239	253,317,697
SPECIAL PROGRAM AREAS [1]									
6. Scientific evaluation grants	650,000	206,000	45,000	15,000	12,000	15,000		30,000	973,000
7. International medical research (Sp.)	500,000	875,000	500,000	875,000		875,000	500,000	875,000	5,000,000
8. Gorgas Memorial Laboratory							750,000		750,000
9. Clinical research centers:									
Therapeutic and metabolic	5,000,000	500,000	500,000	500,000		500,000	500,000	500,000	8,000,000
Categorical		5,500,000	500,000	5,500,000				500,000	12,000,000
10. Primate centers				7,000,000					7,000,000
11. Construction of cancer research facility		5,000,000							5,000,000
12. Total research	45,446,443	50,731,454	31,436,620	57,221,389	5,274,000	41,022,202	30,002,350	30,906,239	292,040,697
13. Balance (+) or deficit (−) (line 1d minus line 12)	−3,602,443	+896,346	+1,488,380	−1,468,389	+503,000	+842,298	−918,050	+658,461	[2] −1,600,397

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[1] Special program areas are shown at allocated levels.

[2] Specific backlog of approved unfinanced grants follows:

G. R. & S.	$3,602,443
Heart	1,468,389
Allergy	918,050
Total	5,988,882

Analysis of 1962 research grants (reflects release of requested unprogramed reserves and release of IRG funds to support regular program in 1961)

	G.R. & S.	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Total
Continuation grants:									
1. The number and amount of continuation grants anticipated for 1962 for which there is a moral commitment	$20,304,000 (1,014)	$27,278,000 (1,433)	$21,106,000 (1,207)	$29,223,000 (1,579)	$3,697,000 (201)	$27,888,000 (1,688)	$18,814,000 (1,274)	$20,450,000 (896)	$168,760,000 (9,292)
2. The number and amount of continuation grants anticipated for 1962 for which there is at present no moral commitment	6,307,000 (315)	8,473,000 (445)	6,556,000 (375)	9,077,000 (491)	1,148,000 (62)	8,662,000 (525)	5,844,000 (396)	6,352,000 (278)	52,419,000 (2,887)
New grants:									
3. The number and amount of recommended but unpaid applications from 1961 (carryover for 1962 reconsideration)	3,602,443 (180)	(--)	(--)	1,468,389 (74)	(--)	(--)	918,000 (64)	(--)	5,988,832 (318)
4. The number and amount of new applications in 1962 estimated to be approved by councils	15,638,000 (918)	10,023,000 (523)	10,711,000 (555)	14,689,000 (893)	1,898,000 (157)	14,387,000 (976)	8,768,000 (628)	9,745,000 (506)	85,859,000 (5,156)
5. Increase for Government share of indirect costs	296,000	288,000	248,000	346,000	46,000	332,000	210,000	234,000	2,000,000
6. Institutional research grants	1,924,000	2,328,000	1,772,000	2,565,000	336,000	2,356,000	1,520,000	1,699,000	14,500,000
7. Subtotal, normal program projection	48,071,443 (2,427)	48,390,000 (2,401)	40,393,000 (2,137)	57,368,389 (3,037)	7,125,000 (420)	53,625,000 (3,189)	36,074,000 (2,362)	38,480,000 (1,680)	329,526,832 (17,653)
Special program areas: [1]									
8. Primate and clinical research centers	13,500,000	7,500,000	500,000	14,000,000		500,000	500,000	500,000	37,000,000
9. Gorgas Memorial Institute							250,000		250,000
10. International medical research (Sp.)	500,000	875,000	500,000	875,000		875,000	500,000	875,000	5,000,000
Other:									
11. Scientific evaluation and planning grants	848,000	270,000	45,000	15,000	15,000	20,000		40,000	1,253,000
12. Total, all projections	62,919,443	57,035,000	41,438,000	72,258,389	7,140,000	55,020,000	37,324,000	39,895,000	373,029,832
13. 1962 revised budget estimate	53,324,000	55,205,000	36,480,000	66,187,000	6,718,000	48,530,000	31,637,000	35,384,000	333,465,000
14. Deficit (line 13 minus line 12)	−9,595,443	−1,830,000	−4,958,000	−6,071,389	−422,000	−6,490,000	−5,687,000	−4,511,000	−39,564,832

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[1] Special program areas are shown at allocated levels.

EXPLANATION OF 1962 BUDGET AMENDMENTS

Mr. FOGARTY. And we will place in the record your formal submission regarding the 1962 budget amendments.

(The material referred to follows:)

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

March 10, 1961

REVISED BUDGET ESTIMATES, 1962—OPERATING APPROPRIATIONS

GENERAL STATEMENT

Introduction

The explanation of increases in the 1962 revised budget estimates over the 1962 original estimates for the operating appropriations of the National Institutes of Health are being presented in summary form.

They have been developed to reflect certain modifications based on experience and program developments during the first half of 1961. The following are factors which have resulted in the requested increase of $43 million over the 1962 original estimates:

1. Reappraisal of requirements for the research projects and special programs, clarification of the impact of the institutional grants program, and decision to increase the Government's share of indirect cost of medical research	$36,707,000
2. Reappraisal of review and approval requirements taking into account projected increases in regular programs and the new special grant programs	1,200,000
3. Reappraisal of requirements for direct research, research contracts, other direct operations activities, and supporting services	5,093,000
Total, increases	43,000,000

A comparison of the 1962 revised budget estimates with the 1962 original estimates follows:

[In thousands]

	1962 original estimates	1962 revised budget estimates	Increase
Grants:			
Research	$296,758	$333,465	$36,707
Fellowships	22,000	22,000	
Training	96,242	96,242	
State control programs	13,000	13,000	
Community demonstration projects	2,000	2,000	
Total, grants	430,000	466,707	36,707
Direct operations:			
Research	61,863	64,112	2,249
Biologics standards	3,025	3,050	25
Review and approval	8,646	9,846	1,200
Training activities	336	336	
Professional and technical assistance	11,575	13,234	1,659
Chemotherapy contracts	21,538	22,538	1,000
Administration	3,017	3,177	160
Total, direct operations	110,000	116,293	6,293
Total, 1962 estimates	540,000	583,000	43,000

Discussion of the estimates

The following is a summary of the increases by activity and an explanation of the general concepts on which the estimates are based.

1. Research grants—Increase $36,707,000

[In thousands]

	1962 original estimates	1962 revised budget estimates	Increase
Regular programs:			
Continuations	$189,927	$189,927	
Supplementals	18,157	18,157	
New grants:			
Carryover	15,353	15,353	
"Wholly" new	18,580	50,025	$31,445
Institutional research grants	12,738	14,500	1,762
Increase for Government's share of indirect costs		2,000	2,000
Subtotal, regular programs	254,755	289,962	35,207
Special programs:			
Scientific evaluation grants	1,253	1,253	
International medical research (special)	5,000	5,000	
Gorgas Memorial Laboratory	250	250	
Clinical research centers:			
Therapeutic and metabolic	12,000	13,500	1,500
Categorical	16,500	16,500	
Primate centers	7,000	7,000	
Subtotal, special programs	42,003	43,503	1,500
Total, research grants	296,758	333,465	36,707

A. Regular grants (including institutional research grants), increase $35,207,000

The increase in the revised estimates for the regular program includes $1,762,000 for expanding the institutional research grants program in 1962. During 1961 and 1962 funds will be made available only to health professions schools. In subsequent years, the program would be extended to provide support to other qualified institutions.

An additional $2 million is requested to provide for increasing the Government's share of indirect costs on regular grants approved on or after January 1, 1962. Presently, congressional authorization provides for the payment of full direct costs of medical research projects and a maximum of 15 percent of indirect costs. It is proposed to support a greater portion of the indirect costs.

The balance of the increase, $31,445,000, would be applied to the additional support of wholly new approved applications including $2 million in programed grants for controlled clinical trial of drugs developed in the chemotherapy program. This additional increment would provide a total amount sufficient to support approximately 58 percent of the wholly new approved applications anticipated in 1962 as compared to only 20 percent which could be financed in the 1962 original estimates.

B. General and categorical clinical research centers, increase $1,500,000

The 1962 original estimates of $28,500,000 included an allowance for clinical research centers of $8,500,000 over 1961. The increase in the revised estimates of $1,500,000 is needed to take advantage of the opportunity for further development of the general metabolic and therapeutic clinical research centers.

2. Direct operations, increase $6,293,000

Requirements for direct operations activities, both Institute programs and supporting services, have been reappraised to assure consideration of the current status of programs.

A. Institute direct research activities, increase $1,242,000

Cancer, $146,000.—Additional funds would be used for the intensification of (1) virus studies, and (2) studies concerned with the application of automation and mathematics to solving laboratory and clinical problems—included in this category are those studies which simultaneously measure the physiological response of patients after surgery and other treatment.

Mental health, $215,000.—The additional funds would support expansion of studies of normal structure and function, both physiological and psychological, which should lead to a greater comprehension of the mechanisms of mental disease, and to more accurate diagnosis and effective treatment. Particular emphasis would be placed on clinical neuropharmacological and biometrics research.

Heart, $430,000.—Primarily these funds would round out the intramural program through support of expanded research with animals and studies on human exercise and fatigue. The animal research, involving expansion of facilities for animal surgery, will refine and develop diagnostic techniques applicable to humans. In addition, funds are included for increased processing and evaluation of biometrical data; extension of epidemiology studies; initiation of industrial population studies; and further development of statistical theory and methodology as applied to biological and medical research.

Dental, $43,000.—This increase will support expansion in clinical investigations oro-pharyngeal neuromotor performance program. This study would provide for the application of available methods of pressure and sound recording to the actions of feeding, swallowing, respiration, and speech.

Arthritis, $102,000.—The increase would permit development of programs in molecular biology and international studies in epidemiology, biometry, and civilian nutrition research.

Allergy, $160,000.—These funds would provide for increases in clinical investigations, tropical virology, and parasite chemotherapy. Extensive increases will be provided in clinical investigations to develop the pediatric service section. Additional staff will be required upon completion of the renovations necessary to facilitate this operation.

Neurology, $146,000.—These funds are required for the expansion of collaborative and field research programs such as perinatal research, biometrics, and epidemiology.

B. Logistical research supporting services, increase $1,007,000

Research supportive services, $524,000.—Approximately one-half of the increase would be required to cover nonrecurring costs associated with the transition to a new computer system, the Minneapolis-Honeywell 800. The balance of the increase would support, commensurate with anticipated research requirements, needed laboratory aids, preventive maintenance, and sanitary engineering services.

Clinical supportive services, $198,000.—An increase is proposed for modifications of existing operating room space, conversion of two nursing units, and increased costs of services for patient care.

Administrative management, $285,000.—The increase would be used to replace essential transportation equipment; rent additional warehouse space; provide additional equipment for radiation and general safety projects; housekeeping and guard services for the new dental building; and expansion of housekeeping, communication, and guard services for the new general office building, now scheduled for occupancy on July 15, 1961.

C. Biologics standards, increase $25,000

The increase would be used for further expansion of the live vaccines program.

D. Review and approval programs, increase $1,200,000

This increase is required for staffing and relating supporting analytical and processing functions in relation to proposed expansion of grants activities. The expansion of these programs, particularly the institutional research grants and the various special centers programs, will require not only routine review and approval services, but also competent program appraisal at a sufficiently high professional level to insure that the research proposals maintain high standards.

E. Professional and technical assistance, increase $1,659,000

An increase of $1,300,000 is required for broader support of recently established studies relating to viruses as the cause of cancer. The rather extensive research services and resources required for this area will be provided primarily through contracts.

The balance of the increase ($359,000) would provide additional medical and nursing officers and other professional personnel to reinforce the small numbers of trained staff directing cancer, mental, and heart community programs in State and local agencies.

F. Chemotherapy contracts, increase $1 million

These funds are required for the expansion of preclinical pharmacology and diversification of the primary screen. Reorientation of the program, both as to scope and points of immediate emphasis, has grown out of judgments made from a definitive review by panels of consultants.

G. Administration, increase $160,000

The 1962 original estimates did not reflect an assessment of the administrative impact of the special program of international medical research proposed and approved in the last few days of the August session of Congress. An increase is requested, therefore, to assure that there would be adequate executive direction of these activities. Additional funds are requested for the Office of the Associate Director for Research Grants to free him of day-to-day operating responsibilities involved in administering the Division of Research Grants.

National Institutes of Health

Revised budget estimates, 1962

Obligations by activity	Management fund	GRS-NIH	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Total
Grants:										
Research		$53, 324, 000	$55, 205, 000	$36, 480, 000	$66, 187, 000	$6, 718, 000	$48, 530, 000	$31, 637, 000	$35, 384, 000	$333, 465, 000
Fellowships		10, 100, 000	2, 400, 000	2, 390, 000	3, 100, 000	760, 000	870, 000	1, 400, 000	980, 000	22, 000, 000
Training		26, 500, 000	7, 055, 000	28, 356, 000	9, 604, 000	3, 291, 000	8, 300, 000	5, 290, 000	7, 846, 000	96, 242, 000
State control programs			3, 500, 000	6, 000, 000	3, 500, 000					13, 000, 000
Community demonstration projects			2, 000, 000							2, 000, 000
Total, grants		89, 924, 000	70, 160, 000	73, 226, 000	82, 391, 000	10, 769, 000	57, 700, 000	38, 327, 000	44, 210, 000	466, 707, 000
Direct operations:										
Research:										
Direct operating funds			7, 776, 000	5, 824, 000	5, 928, 000	1, 982, 000	6, 114, 000	6, 104, 000	5, 388, 000	39, 116, 000
Reimbursements:										
Research supportive services	[1] ($8, 021, 000)		2, 193, 000	1, 184, 000	1, 124, 000	354, 000	1, 387, 000	1, 007, 000	772, 000	8, 021, 000
Clinical supportive services	(10, 900, 000)		2, 883, 000	1, 699, 000	2, 074, 000	153, 000	1, 323, 000	1, 156, 000	1, 612, 000	10, 900, 000
Administrative management	[2] (6, 075, 000)		1, 925, 000	983, 000	774, 000	217, 000	901, 000	711, 000	564, 000	6, 075, 000
Advances for nonformula items	(285, 000)									
Cafeteria	(425, 000)									
Total, reimbursements	(25, 706, 000)		7, 001, 000	3, 866, 000	3, 972, 000	724, 000	3, 611, 000	2, 874, 000	2, 948, 000	24, 996, 000
Total, research	(25, 706, 000)		14, 777, 000	9, 690, 000	9, 900, 000	2, 706, 000	9, 725, 000	8, 978, 000	8, 336, 000	64, 112, 000
Biologics standards:										
Direct operating funds		2, 501, 000								2, 501, 000
Reimbursements	(549, 000)	549, 000								549, 000
Total, biologics standards	(549, 000)	3, 050, 000								3, 050, 000
Review and approval:										
Direct operating funds		1, 065, 000	650, 000	980, 000	679, 000	194, 000	464, 000	383, 000	555, 000	4, 970, 000
Reimbursements	[3] (4, 876, 000)	821, 000	750, 000	777, 000	810, 000	116, 000	586, 000	390, 000	626, 000	4, 876, 000
Total, review and approval	(4, 876, 000)	1, 886, 000	1, 400, 000	1, 757, 000	1, 489, 000	310, 000	1, 050, 000	773, 000	1, 181, 000	9, 846, 000
Training activities				100, 000	186, 000				50, 000	336, 000

Professional and technical assistance:										
NIH			6,381,000	2,803,000						9,184,000
BSS			1,250,000		2,800,000					4,050,000
Total, professional and technical assistance			7,631,000	2,803,000	2,800,000					13,234,000
Chemotherapy contracts			22,538,000							22,538,000
Administration:										
Direct operating funds		448,000	383,000	529,000	191,000	108,000	135,000	121,000	214,000	2,129,000
Reimbursements	(1,048,000)	33,000	278,000	219,000	116,000	40,000	130,000	123,000	109,000	1,048,000
Total, administration	(1,048,000)	481,000	661,000	748,000	307,000	148,000	265,000	244,000	323,000	3,177,000
Outside reimbursements	(465,000)									
Total, direct operations	(32,644,000)	5,417,000	47,007,000	15,098,000	14,682,000	3,164,000	11,040,000	9,995,000	9,890,000	116,293,000
Total, 1962 estimate	(32,644,000)	95,341,000	117,167,000	88,324,000	97,073,000	13,933,000	68,740,000	48,322,000	54,100,000	583,000,000

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[1] Excludes $115,000 in outside reimbursements.
[2] Excludes $176,000 in outside reimbursements.
[3] Excludes $174,000 in outside reimbursements.

Increases in 1962 revised budget estimates over 1962 original estimates

Obligations by activity	Management fund	GRS-NIH	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Total
Grants:										
Research		$7,681,000	$4,794,000	$4,785,000	$4,767,000	$780,000	$6,105,000	$3,563,000	$4,232,000	$36,707,000
Fellowships										
Training										
State control programs										
Community demonstration projects										
Total, grants		7,681,000	4,794,000	4,785,000	4,767,000	780,000	6,105,000	3,563,000	4,232,000	36,707,000
Direct operations:										
Research:										
Direct operating funds			146,000	215,000	430,000	43,000	102,000	160,000	146,000	1,242,000
Reimbursements:										
Research supportive services	($524,000)		143,000	77,000	74,000	22,000	91,000	66,000	51,000	524,000
Clinical supportive services	(198,000)		52,000	30,000	38,000	3,000	25,000	20,000	30,000	198,000
Administrative management	(285,000)		89,000	46,000	36,000	10,000	42,000	34,000	28,000	285,000
Advances for nonformula items										
Cafeteria										
Total, reimbursements	(1,007,000)		284,000	153,000	148,000	35,000	158,000	120,000	109,000	1,007,000
Total, research	(1,007,000)		430,000	368,000	578,000	78,000	260,000	280,000	255,000	2,249,000
Biologics standards:										
Direct operating funds		25,000								25,000
Reimbursements										
Total, biologics standards		25,000								25,000
Review and approval:										
Direct operating funds		109,000	66,000	101,000	72,000	19,000	47,000	129,000	57,000	600,000
Reimbursements	(600,000)	112,000	87,000	90,000	103,000	14,000	73,000	48,000	73,000	600,000
Total, review and approval	(600,000)	221,000	153,000	191,000	175,000	33,000	120,000	177,000	130,000	1,200,000
Training activities										
Professional and technical assistance:										
NIH			1,364,000	24,000						1,388,000
BSS			93,000		178,000					271,000
Total, professional and technical assistance			1,457,000	24,000	178,000					1,659,000

Chemotherapy contracts			1,000,000							1,000,000
Administration:										
Direct operating funds		6,000	8,000	8,000	4,000	2,000	1,000	2,000	4,000	35,000
Reimbursements	(125,000)	4,000	33,000	26,000	14,000	5,000	15,000	15,000	13,000	125,000
Total, administration	(125,000)	10,000	41,000	34,000	18,000	7,000	16,000	17,000	17,000	160,000
Outside reimbursements (all activities)										
Total, direct operations	(1,732,000)	256,000	3,081,000	617,000	949,000	118,000	396,000	474,000	402,000	6,293,000
Total, increases	(1,732,000)	7,937,000	7,875,000	5,402,000	5,716,000	898,000	6,501,000	4,037,000	4,634,000	43,000,000

Original estimates, 1962

Obligations by activity	Management fund	GRS-NIH	Cancer	Mental	Heart	Dental	Arthritis	Allergy	Neurology	Total
Grants:										
Research		$45,643,000	$50,411,000	$31,695,000	$61,420,000	$5,938,000	$42,425,000	$28,074,000	$31,152,000	$296,758,000
Fellowships		10,100,000	2,400,000	2,390,000	3,100,000	760,000	870,000	1,400,000	980,000	22,000,000
Training		26,500,000	7,055,000	28,356,000	9,604,000	3,291,000	8,300,000	5,290,000	7,846,000	96,242,000
State control programs			3,500,000	6,000,000	3,500,000					13,000,000
Community demonstration projects			2,000,000							2,000,000
Total, grants		82,243,000	65,366,000	68,441,000	77,624,000	9,989,000	51,595,000	34,764,000	39,978,000	430,000,000
Direct operations:										
Research:										
Direct operating funds			7,630,000	5,609,000	5,498,000	1,939,000	6,012,000	5,944,000	5,242,000	37,874,000
Reimbursements:										
Research supportive services	[1]($7,497,000)		2,050,000	1,107,000	1,050,000	332,000	1,296,000	941,000	721,000	7,497,000
Clinical supportive services	(10,702,000)		2,831,000	1,669,000	2,036,000	150,000	1,298,000	1,136,000	1,582,000	10,702,000
Administrative management	[2](5,790,000)		1,836,000	937,000	738,000	207,000	859,000	677,000	536,000	5,790,000
Advances for nonformula items	(285,000)									
Cafeteria	(425,000)									
Total, reimbursements	(24,699,000)		6,717,000	3,713,000	3,824,000	689,000	3,453,000	2,754,000	2,839,000	23,989,000
Total, research	(24,699,000)		14,347,000	9,322,000	9,322,000	2,628,000	9,465,000	8,698,000	8,081,000	61,863,000
Biologics standards:										
Direct operating funds		2,476,000								2,476,000
Reimbursements	(549,000)	549,000								549,000
Total, biologics standards	(549,000)	3,025,000								3,025,000
Review and approval:										
Direct operating funds		956,000	584,000	879,000	607,000	175,000	417,000	254,000	498,000	4,370,000
Reimbursements	[3](4,276,000)	709,000	663,000	687,000	707,000	102,000	513,000	342,000	553,000	4,276,000
Total, review and approval	(4,276,000)	1,665,000	1,247,000	1,566,000	1,314,000	277,000	930,000	596,000	1,051,000	8,646,000
Training activities				100,000	186,000				50,000	336,000
Professional and technical assistance:										
NIH			5,017,000	2,779,000						7,796,000
BSS			1,157,000		2,622,000					3,779,000
Total, professional and technical assistance			6,174,000	2,779,000	2,622,000					11,575,000

Chemotherapy contracts			21, 538, 000							21, 538, 000
Administration:										
Direct operating funds		442, 000	375, 000	521, 000	187, 000	106, 000	134, 000	119, 000	210, 000	2, 094, 000
Reimbursements	(923, 000)	29, 000	245, 000	193, 000	102, 000	35, 000	115, 000	108, 000	96, 000	923, 000
Total, administration	(923, 000)	471, 000	620, 000	714, 000	289, 000	141, 000	249, 000	227, 000	306, 000	3, 017, 000
Outside reimbursements (all activities)	(465, 000)									
Total, direct operations	(30, 912, 000)	5, 161, 000	43, 926, 000	14, 481, 000	13, 733, 000	3, 046, 000	10, 644, 000	9, 521, 000	9, 488, 000	110, 000, 000
1962, original estimates	(30, 912, 000)	87, 404, 000	109, 292, 000	82, 922, 000	91, 357, 000	13, 035, 000	62, 239, 000	44, 285, 000	49, 466, 000	540, 000, 000

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[1] Excludes $115,000 in outside reimbursements.
[2] Excludes $176,000 in outside reimbursements.
[3] Excludes $174,000 in outside reimbursements.

History of NIH Appropriations

Mr. Fogarty. We will also place in the record the usual history of NIH appropriations from 1938 to date.
(The information referred to follows:)

Appropriation history, National Institutes of Health

Appropriation title	1938	1939	1940	1941	1942	1943	1944	1945	1946
General research and services, National Institutes of Health:[1]									
Obligational cash	$64,000	$64,000	$137,000	$141,000	$135,000	$743,400	$2,025,020	$2,274,000	$2,866,000
Salaries, expenses and grants, National Cancer Institute: Obligational cash	400,000	400,000	570,000	570,000	565,000	534,870	530,000	561,000	548,700
Total, obligational cash	464,000	464,000	707,000	711,000	700,000	1,278,270	2,555,020	2,835,000	3,414,700

Appropriation title	1947	1948	1949	1950	1951	1952	1953	1954
General research and services, National Institutes of Health:[2]								
Obligational cash	$6,254,548	$10,126,000	$14,540,000	$12,075,000	$14,313,900	$15,756,500	$16,598,750	$4,675,000
Contract authority				1,925,000				
Salaries, expenses, and grants, National Cancer Institute:								
Obligational cash	1,820,900	14,500,000	14,000,000	14,725,000	15,086,000	15,031,750	17,887,000	20,237,000
Liquidation cash				4,175,000	5,000,000	4,625,000		
Contract authority			8,000,000	6,000,000				
Mental health activities:								
Obligational cash		[3] 4,250,000	[3] 9,128,000	[3] 10,862,000	7,130,000	9,988,737	10,895,000	12,095,000
Liquidation cash				750,000	2,375,000	573,000		
Contract authority			2,300,000	2,150,000				
Salaries, expenses and grants, National Heart Institute:								
Obligational cash				10,725,000	8,850,000	10,082,650	12,000,000	15,168,000
Liquidation cash					5,350,000			
Contract authority				5,350,000				
Dental health activities: Obligational cash				1,780,000	1,954,850	1,617,654	1,650,000	1,740,000
Arthritis and metabolic disease activities: Obligational cash								7,000,000
Allergy and infectious disease activities: Obligational cash								5,738,000
Neurology and blindness activities: Obligational cash								4,500,000
Total:								
Obligational cash	8,075,448	28,876,000	37,668,000	50,167,000	47,334,750	52,477,291	59,030,750	71,153,000
Liquidation cash				4,925,000	12,725,000	5,198,000		
Contract authority			10,300,000	15,425,000				

Appropriation title	1955	1956	1957	1958	1959	1960	1961	Estimate, 1962
General research and services, National Institutes of Health: Obligational cash	$4,675,000	$5,929,000	$12,122,000	$14,026,000	$28,974,000	$45,994,000	$83,900,000	$95,341,000
Salaries, expenses, and grants, National Cancer Institute: Obligational cash	21,737,000	24,978,000	48,432,000	56,402,000	75,268,000	91,257,000	111,000,000	117,167,000
Mental health activities: Obligational cash	14,147,500	18,001,000	35,197,000	39,217,000	52,419,000	68,090,000	100,900,000	88,324,000
Salaries, expenses, and grants, National Heart Institute: Obligational cash	16,668,000	18,898,000	33,396,000	35,936,000	45,613,000	62,237,000	86,900,000	97,073,000
Dental health activities: Obligational cash	1,990,000	2,176,000	6,026,000	6,430,000	7,420,000	10,019,000	15,500,000	13,933,000
Arthritis and metabolic disease activities: Obligational cash	8,270,000	10,840,000	15,885,000	20,385,000	31,215,000	46,862,000	61,200,000	68,740,000
Allergy and infectious disease activities: Obligational cash	6,180,000	7,775,000	13,299,000	17,400,000	24,071,000	34,054,000	44,000,000	48,322,000
Neurology and blindness activities: Obligational cash	7,600,500	9,861,000	18,650,000	21,387,000	29,403,000	41,487,000	56,600,000	54,100,000
Total, obligational cash	81,268,000	98,458,000	183,007,000	211,183,000	294,383,000	400,000,000	[4] 560,000,000	583,000,000

[1] Appropriation title changed from "Operating expenses" in 1958.

[2] The "General research and services" appropriation provided unidentifiable amounts in the initial years of the "Arthritis and metabolic disease activities," "Allergy and infectious disease activities," "Neurology and blindness activities," and the "National Heart Institute."

[3] Includes funds for support of narcotic hospitals at Lexington and Fort Worth which were subsequently transferred.

[4] Includes funds for construction of mental health-neurology research facility.

History of congressional action on budget requests for NIH

Year	Budget request			Appropriation		
	Obligational cash	Liquidating cash	Contract authority	Obligational cash	Liquidating cash	Contract authority
1932	$48,000			$48,000		
1933	48,000			48,000		
1934	54,775			54,775		
1935	50,000			50,000		
1936	64,000			64,000		
1937	64,000			64,000		
1938	464,000			464,000		
1939	515,000			515,000		
1940	587,750			707,000		
1941	712,120			711,000		
1942	705,000			700,000		
1943	1,278,270			1,278,270		
1944	1,291,000			2,555,020		
1945	2,835,000			2,835,000		
1946	2,078,000			3,414,700		
1947	10,799,500			[1] 8,125,448		
1948	22,403,000			28,876,000		
1949	45,701,460		$2,300,000	37,668,000		$10,300,000
1950	40,567,000	$3,900,000	3,595,000	50,167,000	[2] $4,925,000	15,425,000
1951	49,845,000	12,725,000		[3] 47,334,750	12,725,000	
1952	53,386,000	5,648,000		52,477,291	5,198,000	
1953	55,005,000			59,030,750		
1954	56,340,000			71,153,000		
1955 [4]	71,128,000			81,268,000		
1956 [5] [6]	90,023,000			98,458,000		
1957 [5]	[7] 126,725,000			183,007,000		
1958	190,183,000			211,183,000		
1959	211,814,000			294,383,000		
1960	294,279,000			400,000,000		
1961	400,000,000			[8] 560,000,000		
1962	583,000,000					

[1] Includes $386,500 transfers.

[2] Not less than $3,000,000 was earmarked for liquidating cash; an additional $1,175,000 was used for that purpose.

[3] Excludes $3,216,250 rescinded.

[4] Excludes $131,000 for Gorgas Memorial Laboratory.

[5] Excludes $147,000 for Gorgas Memorial Laboratory.

[6] Includes $90,000 transfer.

[7] Includes $200,000 transfer from other appropriations.

[8] Includes $12,139,000 for construction of mental health-neurology research facility.

NOTE.—Not all amounts in this table are comparable from year to year because of inconsistencies in the content of the appropriations. Prior to 1938 they exclude all salaries. Prior to 1943 they exclude all salaries other than those of employees of the National Cancer Institute. Prior to 1949 they exclude pay of regular corps officers. For 1948, 1949, and 1950 they include funds for support of narcotic hospitals at Fort Worth and Lexington which were subsequently transferred.

USE OF FUNDS APPROPRIATED IN EXCESS OF THE 1961 BUDGET

Mr. FOGARTY. Last year the Congress gave you an appropriation that was $160 million more than you requested. Does it now appear that practically all of these funds will be used to good advantage?

Dr. SHANNON. Practically all, yes, sir. There will be an unobligated balance, after adjustment of reserves, of what?

Mr. SEGGEL. $4 million.

Dr. SHANNON. $4 million, roughly.

Mr. SEGGEL. If we get the additional apportionment which we have requested of the Budget Bureau.

Mr. FOGARTY. Well, if you get the apportionment request that you made to the Bureau of the Budget and institutional grants are not allowed this year, you will have what, $4 million?

Mr. KELLY. It would be about $5,800,000——

Mr. FOGARTY. With no institutional grants?

Mr. KELLY. If the reserves were released as needed.

Mr. Fogarty. Is there any reason for your having left out any information on institutional grants in the justifications? You do not spend much time on it or give much specific information in the justifications, I notice.

Dr. Shannon. No, there was no reason. If it was not taken up at sufficient length, then that was an error on our part. Certainly it is not a reflection of our feeling of their importance, as I indicated this morning.

Mr. Fogarty. I understand. There were still questions to be settled in the executive branch when these were prepared.

FOREIGN FELLOWSHIP PROGRAM

How is the foreign fellowship program working out?

Dr. Shannon. That is working out very well, and it is having results to the effect that we had hoped. Let me review the development that was started 4 years ago, and implemented 3 years ago.

This is not a separate program, but is conducted as part of our general fellowship program. Prior to the Korean war, we made available a very limited number of fellowships to citizens outside of the United States. The present program is an extension into today's activities of that part of the pre-Korean program that is concerned with fellowships for a limited number of individuals, not citizens of the United States. We started, initially, with 15 from the Western European countries, and have now expanded this number during subsequent years to about 90 awards.

These fellows are nominated by scientific groups, composed of scientists within the country. Represented are 33 countries. Most of these are countries with which we have normal conventional scientific interchanges.

The fellows are selected by what amounts to national competitions. In many cases this is an advertised competition. They are nominated to us in groups of two to four by the national body.

For instance, in the United Kingdom program the nominating group is the Medical Research Council—and this has its counterparts in Sweden and Germany. Of those nominated, we make a selection within whatever limit is determined. As I say, this year it is 90.

These fellows come to the United States to an institution where prior arrangements have been made for them to study. The selection depends in part on the general excellence of the individual, in part upon his specific scientific discipline. One of the big advantages to our country in this program is to intermix with our graduate students some of the really brilliant people from overseas who derive from a different culture, and who have a different academic background. These individuals, in general, stay here for 1 year, although they can apply for renewal. We have very few requests for renewal.

The manner of their selection assures that they will have very good scientific facilities on their return. We have a provision in our program, to make small grants to the fellows on their return if these are needed to develop their laboratories. In this manner they can form effective nuclei for the development of science along the lines of their training experience in their own nation. We have found very little need to use large quantities of money for this type of thing.

We are now in the process of following these up, individual by individual, both directly and through the institution that was their host during their year's residence in this country. In this way we will obtain a clearer appraisal of how they are evolving as compared to their counterparts out of the country.

Mr. Fogarty. Are you satisfied with their progress?

Dr. Shannon. I am very well satisfied, sir.

And I would point out that these fellowships are among the most prized fellowships in international competition. Heretofore, the most desirable fellowship, a biologist or a medical scientist could obtain—and, in fact, this is still the case—was one of the foreign Rockefeller fellowship awards. The fellows that are now applying and successfully competing for Rockefeller fellowships are no better or worse than the fellows we are obtaining in this program.

In point of fact, we are following the conventions that were developed by the Rockefeller Foundation, because it is our conviction, after careful study of foreign programs, that the Rockefeller Foundation, over the years, has evolved mechanisms that are as close to perfection as those of any granting agency, whether it be inside or outside of government.

I might add that the Rockefeller Foundation itself has been very, very helpful in assisting us to develop, within the scientific environment abroad, the selection committees and by giving us guidance in their evolution. This has taken considerable time on the part of the foundation staff members, and I think that the success of the program is in no small measure due to their willingness to help.

I might point out that we have had additional help from the Kellogg Foundation, the Pan-American Health Organization, and the International Cooperation Administration.

And the reason why these organizations have been so forthright in their willingness to help is that they are as convinced as we that this is a special type of program that satisfies a need that is not satisfied by the ICA program, the Fulbright awards or any of a number of other awards.

The direct benefits, I think, are that we now have a series of scientists of very superior caliber spread throughout the world, who have had a very broad experience in the United States and have seen U.S. science as it exists, as it develops, and have a very clear picture of what the science community of the United States is. But they have also had a very clear picture of the United States as a social entity, as a country. I think they are in a better position to appraise our strength and our weaknesses. And I think that this appreciation of our culture will be of great indirect benefit to us.

VARIATION IN SPECIAL FELLOWSHIP AWARDS

Mr. Fogarty. Why is there so much variation between the institutes in the average amount awarded per fellow in some programs. For instance, the special fellowships vary—$7,166 for dental; $7,500 for heart; $8,500 for arthritis; $9,500 for mental; and $10,200 for cancer?

Dr. Shannon. Well, I cannot give you any special reason. Special fellows as such are—well, special in the sense that they are apart from the normal fellowship programs, are not handled en masse but are handled as individual fellows who are given support to attain a very specific objective that cannot be attained by the normal research branch. And, in general, they are considerably more senior than the postdoctorate fellow. I could give you a detailed breakdown, which I would be glad to do.

Mr. Fogarty. Mr. Denton.

VIRUS ANTIGENS

Mr. Denton. There is just one question that I want to ask. That is about measles.

I think it was last year someone talked about cancer being caused by virus in certain cases, and they said there were antibodies but the antibodies could not get at the virus because the virus was inside the cell. Well, is that not the same condition with the measles?

Dr. Shannon. Well, it is only partly true in both cases, because the virus, in order to have its effect, must multiply and go from one cell to the other; and, although it is not exposed to an antibody circulating in the plasma fluids during the period of growth in the cell, it is exposed to the antibody in its transition from one cell to another. This very short time of exposure is true of all viral diseases. The more important fact is that this virus does not constitute an independent viable entity that can exist of itself and grow outside of the cell, it is a simple organism.

Mr. Denton. The antibody gets at the virus when it goes from one cell to another?

Dr. Shannon. Yes, sir. The antibody interposes itself as a barrier in the movement of the virus from one cell to another. The virus cannot multiply outside the cell.

Mr. Denton. Why can they not get some kind of cancer vaccination, then, if that is the case, if it is a virus?

Dr. Shannon. Well, in point of fact, I would like Dr. Mider, who has a very special knowledge in this field, to comment on that.

Mr. Denton. Maybe I had better bring that up later.

Dr. Shannon. Well, Dr. Mider is right there, if you would like him to comment.

There is a large field of immunology that has evolved in the field of cancer research, and maybe Dr. Mider can summarize it.

Dr. Mider. Mr. Denton, there are a substantial number of viruses which produce specific types of cancer in a variety of experimental animals. As of today, we have not identified any virus which produces cancer in man, although I think most of us are confident that this is a most profitable line of research.

Now, among the viruses that affect chickens or mice, for example, there are some which produce antibodies readily and active immunity against the infection from those viruses can indeed be produced.

On the other hand, there are some which are so weakly antigenic that we are not able to produce sera, antisera against them, by which means we may tell the difference, for example, between two mouse viruses which produce leukemias.

So that just because a virus produces a disease does not necessarily mean that the virus is antigenic enough to provide an effective antiserum or effective means of actively immunizing the antibody against that virus in the light of our present knowledge. But this will probably come.

Mr. Denton. When I asked this, somebody told me that is why you could not get a serum, because the virus was in the cell.

Dr. Mider. That is a part of the picture. But when we are infected by these agents, we have active antibodies, and it is highly probable that the virus would not get in the cell at all. It would be killed before it could get in the cell.

Mr. Denton. That is all.

Mr. Fogarty. Mr. Marshall.

COMPOSITION OF NET INCREASE FOR 1962

Mr. Marshall. Dr. Hunt, your summary statement that you presented to the committee is a matter of the record.

In that statement, you state:

> In conclusion, Mr. Chairman, the amended request for the Division of General Medical Sciences for 1962 is a total of $92,291,000 as compared with the adjusted appropriation of $73,758,000 for 1961.

If my subtraction is correct, that difference would be $18,533,000 between those two figures. Would that be correct?

Dr. Hunt. I have not done the subtraction myself.

Mr. Marshall. Then how did you arrive at the figure in the next sentence of your statement where you say that you have an increase for research grants of $18,559,000? That would be a larger figure than the difference between those two total figures for 1961 and 1962.

Mr. Kelly. Perhaps, Mr. Marshall, I can help you in that. There were some reductions in this account in the amount of $1.5 million. The bulk of this related to funds made available by the Congress in 1961 to permit the advance payment of training grants so that we could move on to a 1-year-in-advance basis, and that was a nonrecurring cost. So the gross increases add up to more than the net increases.

Mr. Marshall. So that these figures are actually not related to the budget requests.

Mr. Kelly. They are the gross increase, and there is an offsetting decrease that brings you to the difference between the appropriations. And I believe that accounts for it.

Dr. Hunt. The comparative transfer to the Bureau of State Services was included in making this adjusted appropriation total, but not the nonrecurring $1.5 million.

Mr. Marshall. In each one of these items following that, is there any decrease—$35,000 for overall planning, and $241,000 for central service costs, and $198,000 for review and approval for professional and clerical staff engaged in processing?

Mr. Kelly. No. I think those are all gross increases. There were just three nonrecurring items.

Mr. Marshall. So you assure me that, after you take off these items, the difference then actually is the $18,533,000?

Mr. Kelly. That is my understanding. I would like to check it. If I am wrong, I will call it to your attention.

Mr. Fogarty. Mr. Laird.

Mr. Laird. Mr. Chairman, we are in the area of general questions now?

Mr. Fogarty. Yes.

INSTITUTIONAL GRANTS

Mr. LAIRD. Dr. Shannon, I would like to ask you about this whole area of institutional grants.

COST

It would seem to me that more funds would be made available under this system of grants than under the individual grant basis. Would you not be using more money in this particular area, a much larger proportion of your overall grants funds, as time passes?

Dr. SHANNON. Oh, yes, sir. We would. At the present time we would view the beginning year as being approximately 5 percent of the total.

Dr. LAIRD. Five percent of the total the first year?

Dr. SHANNON. Yes, sir. And then over a 3- or 4-year period, growing up to 15 percent?

Mr. LAIRD. Growing up to 15 percent?

Dr. SHANNON. Yes, sir.

Mr. LAIRD. Would a comparable reduction be made in the individual grants?

Dr. SHANNON. It may or may not; this will be determined, as these programs become implemented, and the increases in funds we may get in the future.

Mr. LAIRD. Well, will the individual research grants go down?

Dr. SHANNON. In some cases they will disappear completely. For instance, in this——

Mr. LAIRD. What about the whole area as far as the amount of money going into the individual grants and into the institutional grants?

Dr. SHANNON. First, let me take certain areas that will disappear. We will stop making available, in all areas save mental health, the small grants program. These are grants that make available up to $2,000 for the somewhat less extensive project. This is not a large sum, but this is something we will expect the schools to fund out of the institutional grant.

This institutional grant will also be reflected in the quality of applications for research funds because it will enable an institution to fund certain things that are perhaps in the trial period. In other words, we will get research grant requests at a later date than we normally would because the availability of flexible funds will permit the institution to initiate investigations in the light of its best judgment of a man's special capabilities and of unusual experimental opportunities. Having thus demonstrated feasibility and worthwhileness, we would expect, in general, that requests for more stable support would come to us.

We would hope that a substantial proportion of these funds would go into faculty positions. Insofar as faculty positions are paid out of these funds, they would not be chargeable against the research grant. We would also hope that certain resources can be handled on a centralized basis—I mean, for instance, the possibility of central animal production and the possibility of central animal care for research purposes and the like.

These should be normal charges against this type of fund.

Now, it will be difficult for us to tell you, after this operation has been going for 4 or 5 years, what have been the specific advantages of funds expended this way. What we will be able to tell you is that certain individuals, by name or categories, have been supported in their research activities during the period of time; that a certain number of students or a certain number of predoctorate fellows have been supported out of these funds; that certain centralized resources have been developed which have been used by X million dollars worth of grants within the institution and have facilitated their work; and that they have been able to create so many stable faculty positions from the funds. It is this type of information, which will not be highly specific or precise, that will be available.

We will not be able to look at this 15 percent of our research-grant funds, if that is what it will come to be, and say that these funds have produced these results, whereas the remainder have produced the other results. These funds will be effective only insofar as the institution itself can achieve some fluidity and some independent means of determining its own future and use this almost as a revolving fund to develop its total program. If they do that, then they will be used effectively.

LEGISLATIVE HISTORY REGARDING COST

Mr. Laird. Well, what I am trying to get at here, Dr. Shannon, is that it was indicated last year when this bill was up on the floor of the House of Representatives that this particular program would not cost the Federal Government one additional penny.

Dr. Shannon. I think this is correct, sir.

Mr. Laird. Well, it is hard for me to follow the logic of such a statement. I would think that there would be more people putting in applications, and with this kind of authority you would be spending more money than you presently are, if you looked at even a year or 2 years from now.

Dr. Shannon. Well, I would like to make two comments on that.

In the first place, as one budgets these funds, they will have the appearances of costing more in any one budget year as the program builds up. Because if there were institutional grants of the $12 million we are requesting for use in 1961, that is for expenditure by the institution in 1962, that would have no influence on the research grant application that came before us this year.

Mr. Laird. Well, it does not seem to me that you are going to be cutting back on the research grant applications by the amount of money you put into this program. In my opinion it is certain that the Federal Government is going to spend more money.

Dr. Shannon. Let me take the next step. It will not affect any research grant application we will have received this year or we will have acted on. On the other hand, going into the next year, certain salaries that would normally have appeared on research projects, would now, we hope, be charged against the institutional grants. Certain fellowship grants that would appear in the budget will now appear in the institutional grants. Certain of the research grant proposals that would normally come to us next year will not come to us but will be supported by the local institution and thus not require independent Federal financing.

In this sense the money that would be expended this year in making institutional grants available would satisfy certain of the needs the following year.

Now, the thing that is hard for us to demonstrate, I know we will not be able to demonstrate, is that this has not cost the Federal Government every dollar that is put into it as an "add-on" to the research process. But if we adhere to the principle that no dollar of institutional grants can be spent here that is not spent for research or research training purposes; if they are limited to institutions of substantive worth—and this will be determined by the unavailability of these grants to institutions with research programs of less than about $100,000—then if these things are done, the grants will provide a different means for supporting the same work, but will not increase the work supported.

Mr. Laird. How do you handle overhead?

Dr. Shannon. That would be handled in precisely the same way as any other research grant.

Mr. Laird. There is no way that overhead costs can be included in these institutional grants above the 15 percent figure?

Dr. Shannon. No, sir.

Mr. Kelly. Not as long as the limitation applies. Your limitation applies to all research grants.

Mr. Laird. This passed by unanimous consent, on August 30. The debate is carried on page 1722 of the Congressional Record, and the House was assured that there would be no additional cost involved.

These are obviously more attractive than the individual grants. When you have a more attractive program, it would seem to me that you would get a higher cost from that factor alone. You are going to get more pressure for more grant funds. Now, I want to see why that is not true, if it is not. Maybe I am wrong.

SATISFACTION OF NEW NEEDS

Dr. Shannon. Well, I think it is more attractive because it satisfies a need that cannot be satisfied in any sense by a project grant system.

Mr. Laird. Well, does it not stand to reason that if this is going to meet a new need that there will be new costs?

Dr. Shannon. It is going to satisfy a need because it promises to be an adequate way to offset the encroachment of the grants system. These are needs that are not being met.

For instance, we are now preparing a large number of senior scientists—I am not talking now about those that are ready for professional training, I am talking about the person in the middle grades at the assistant or associate professor level. Institutional grants would permit an institution to make appointments for 5 or 8 years at this intermediate level so that a man would know he had stable support for his own personal activities for this period of time and could set his pace accordingly.

Now let me point out that, at the present time, the salaries many of these people receive are solely derived from project grants. If he gets into a period in which his research ideas are not productive, he cannot drop his research activity, short of dropping the entire research grant, which he cannot do because his salary is contained in it.

So, in general, what he will attempt to do is to maintain research productivity as best he can during that period of time, if only to maintain his position within the school.

Now, this is something that we cannot inquire into, but, nevertheless, this is something that, we know, happens.

In other words, this takes the pressure off the scientist to produce even during a nonproductive period and diminishes the cost of carrying him during the period when he is not productive.

Mr. LAIRD. I don't see where there would be much in diminished costs. The more we talk about this the more I am convinced it will cost more money.

Dr. SHANNON. In our justification to the Department we did not present this as a moneysaving device. We presented this as an essential new mechanism to do the job that we were trying to do with the project grants.

What we did point out to the Department was that this was not wholly adequate. Actually, in the composition of our budget—to show you the extent of that—we said that during the initial stage we do not think that more than 25 percent of the institutional grants can be regarded as a probable deduct from the normal research grant application.

We said that we think that at a later time more will be needed, but that during the initial stages 75 percent of these will be straight add-on funds, 25 percent will be substitutive. These are our estimates.

Now, I do feel, on the other hand, that when the program is on a stable level, the bulk of the institutional grant will be substitutive; but substitutive by a technique that performs functions we cannot do adequately with the project system.

Mr. KELLY. Let me explain it. There are two ways to look at it. I think it was unfortunate that the statements were so categorically made that it would not cost any money, although it is a true statement, if it is looked at in this way.

The thought was that out of any given level that was determined would be provided to support grant research, a higher priority should be given to the institutional grants out of that fund than to individual research project grants because of the value to be obtained from them, that a given percentage would be put into them. In this sense, then, if you determined that the research grant area should be $300 million, the making of an institutional grant does not cost you any more than the $300 million. You have merely used a part of the $300 million for this purpose.

Now, if, instead of determining $300 million as a program level, you were making a computed requirement of all applications, then you might arrive at a different result.

COST OFFSETS

Now, the other way in which you can visualize the cost—and I do not think you will get 100 percent offset in costs, but we do know we will get some offset in costs—is that it is anticipated that the institutional research grant will pay for certain costs now being borne by individual project grants, such as senior professors that they want to give tenure to; equipment that is now purchased for an individual project, which the institution would buy for the benefit of a number of projects; and the use of the small project grant for the payment of graduate students in the conduct of research work.

You can enumerate a series of offsets. They may never equal 100 percent, but in the one sense the proposal as made is not costing any more money, on the theory that it was a priority use of the amount of funds determined to be available for the total research grant program.

I do not know whether that helps or not, but it is the concept which I have obtained.

OVERHEAD

Mr. LAIRD. Well now, how does the overhead figure into an institutional grant? It would seem to me that the overhead costs in an institutional grant would be considerably below 15 percent.

Dr. SHANNON. Well, if we insist that nothing can be paid out of the institutional grant that would not normally be, by one device or another, payable out of a project grant—or put it another way: nothing can be paid out of the institutional grant that does not conform to the definition of what constitutes direct research costs in the Bureau of Budget's Circular A–21—then it will cost institutions money to utilize those funds. However, they may be used in precisely the same way as the basic grant in the project system. And it was for this reason that we were led to believe that wherever overhead should go on the regular project grants, it probably should go on this.

Now I might say that there is another thing that is important here. If this is not the case, then this program can be unwisely viewed as just another way to push up indirect costs. And this is not our idea of this at all.

Mr. LAIRD. What about the proposals that you have before you now? What is overhead running in those proposals?

Dr. SHANNON. Well, all these proposals will carry, on the average, 15 percent overhead; most of them will carry 15 percent, no more; some will carry less. If a proposal has a very large element of renovation or very large element of large equipment purchase, then the overhead will be cut down proportionately. But in the average grant the overhead will be 15 percent.

USE OF INSTITUTIONAL GRANTS FOR RENOVATION OF BUILDINGS

Mr. LAIRD. Let us talk a little bit about these institutional grants and the area of renovation of facilities. I would like to discuss that with you a little bit.

What would you consider as renovation in an institutional grant? Would you get in the area of space modification, or strictly renovation?

Dr. SHANNON. Well, quite frankly, we have not clearly defined in our minds what constitutes "space modification" in the sense that you use it and what constitutes "renovation" in the sense that we use it.

Mr. LAIRD. Well, I would like to find out how you define it. That is why I am asking the question.

Dr. SHANNON. Well, I think, that under the term "renovation," we use a combination of terms that in the aggregate add up to renovation—repair and equipment. All of this is under the general heading of making ready a space that will be occupied by a research project. Now, in general, this is minor renovation, however one defines it—you may move one wall or put a string of laboratory benches in.

Mr. LAIRD. Pick out one of those grants that has some renovation in it. You have got some proposals before you now.

Dr. SHANNON. You are now in the area of the clinical research centers.

Mr. LAIRD. No, I am in the area of institutional grants. I understand that you are talking about renovation.

Dr. SHANNON. No, for institutional grants we have no applications yet.

Mr. LAIRD. You have no applications before you at all?

Dr. SHANNON. No, sir.

Mr. LAIRD. So you are not going to need authority this year for institutional grants?

Dr. SHANNON. Well, we are requesting authority to use part of these funds, to the extent of $12 million, to start the program this year. But since the authority came after the appropriation, we did not feel we have the authority to go forward.

Mr. LAIRD. And you have no applications before the National Institutes?

Dr. SHANNON. No formal applications. We had a lot of letters, but no formal applications.

Mr. LAIRD. I wanted to discuss what you meant by renovation in institutional grants. You used the term "renovation" when you were talking about these overhead costs. I will talk about the clinical centers a little later.

Dr. SHANNON. I would think that our position would have to be, on this problem of what constitutes space modification or renovation, that it is not the intent to treat research grants as utilities and construction funds and things that would normally come from another appropriation are treated. That would not be suitable expenditure under this.

On the other hand, I think that we would permit remodeling of animal quarters or the purchase of new cages for animal quarters. We would permit, for instance, the air conditioning of animal quarters, if this was found to be quite essential to the raising of hybrid strains of mice and rats and things like that. We would permit renovation or replacement, quite frankly, of fixed or large equipment of the sort that would quite normally come under the general term "renovation".

Mr. LAIRD. What about taking an old classroom building on the campus?

Dr. SHANNON. This I do not think is suitable for an institutional research grant.

Mr. LAIRD. You would not cover that in this particular appropriation?

Dr. SHANNON. No, sir. I think we get in the problem of renovation, in the sense you want to talk about it, in terms of clinical centers.

Mr. LAIRD. We can talk about that later. I just want to talk about these institutional grants now.

Dr. SHANNON. Yes. We would not permit, much less encourage, the expenditure of any substantial sum for renovation unless this is tied to a specific project that has been considered by an advisory group such as the Council and was felt to warrant a high priority; and, in addition, funds for the renovation should be provided in addition to funds for the maintenance of the operation. These would have to be specific judgments, in our mind.

RENOVATION UNDER REGULAR RESEARCH GRANTS

Mr. Laird. But renovation, under the grants that you have been making for research have been considered part of the direct costs of the research grants?

Dr. Shannon. Yes, because they are made in relation to a defined research objective, a defined scope.

Mr. Laird. And you have felt that it was not necessary to have a policy for schools to contribute anything in that area?

Dr. Shannon. Well, the problem there is that the school is making a very large contribution. In contrast to new construction, where you start from scratch with nothing, the school is contributing very broadly to the overall project. It is contributing the housing, the basic utilities, and all those things that make this particular space modification possible.

But these are elements that are very difficult to cost: whereas it is quite easy to cost a new structure where you can start from wherever the soil lines go to and take from there up to the finished product. This is an architectural entity that is costed as a new structure. And you can get a precise definition of the cost and a sharing of the cost.

But when you go into an old building and convert it so that a new research investigator can occupy it—it seems to us, quite frankly, Mr. Laird, that this can be a very small renovation. In a $10,000 program all it may do, as it has quite frequently done in the past, is to turn a closet into a rat room.

When you go up to very large projects, there is no natural cutoff point that says: from here on this no longer falls in this category but is now a new program: this now is no longer renovation, this is space modification and therefore requires separate authority.

Our concept of the use of these funds is that, if the space adjustment or modification, renovation, repair, or equipment is related to a discrete approvable project that has come before the Council, which considered the funds necessary for repair and improvement and equipment at the same time that they considered the objective of the program and the total budget of the program, then, we feel that, in order to get this work underway, the deficiency must be met. Then this is a contribution by this Council to the support of the work.

The contribution of the school is very difficult to assess in any of these programs. The professor's salary, for example, will in many instances be paid by the school. And in trying to get an accurate measure of the sharing of costs within a project, whether it has to do with renovation of space or the conduct of research, is almost impossible.

FEDERAL CONTROL OVER GRANTS

Mr. LAIRD. Dr. Shannon, I notice in your statement, where you talk about the consolidation of small project grants, you make the statement that—

> If the research done by a medical school, a university department, a hospital, or other research organization is regarded as worthy of governmental support, its research administrators are also worthy of the Government's trust.

Dr. SHANNON. Yes, sir.

Mr. LAIRD. Now, what does that mean? Does that mean that we should not question them, or what does this mean?

Dr. SHANNON. Well, perhaps it is not well stated.

But what was intended is this: If an environment is selected as warranting research support, perhaps under four different research grants, and we depend upon the institution to furnish the backdrop against which this work will be effective—in terms of facilities, services and the like—then, if this work has existed in stable fashion over a given number of years, we really have developed a situation in which we can trust the administrative head of the scientific group to make decisions affecting these four units, within the overall project that has been approved, instead of insisting on individual approval in respect of each of the four individual units by our Study Section groups and Council meetings.

In other words, if we cannot depend upon the wisdom of the scientific leader who is responsible for these four projects, then we probably cannot depend upon him to provide the conditions under which any one of the projects can go forward.

It is not the Government's trust in the accountant's sense, but really that we should trust their scientific judgment in the continuous overseeing of the funds so that fiscal accountability can be pushed back a step from the project leader to the department head.

RECOMMENDED REPEAL OF SECTION 433(a) OF THE PUBLIC HEALTH SERVICE ACT

Mr. LAIRD. What do you think the greatest needs are in medical research as we face the next 3 years?

Dr. SHANNON. Well, sir, I think they are three. I think they are research facilities; I think they are career positions; and I think they are institutional stability.

Mr. LAIRD. What do you think should have priority of the three that you have mentioned?

Dr. SHANNON. Most acutely, research facilities.

Mr. LAIRD. Well, Dr. Shannon, I would like to know why you recommended the repeal of section 433(a) of the Public Health Service Act.

Dr. SHANNON. Put it this way. I agreed that this was advisable. I thought that our overall construction program fell into two general categories. The first category would include the provision of space for research that was specifically definable in terms of program objectives; and the second category would include more general support for a very broad program area that might satisfy a multiplicity of program needs.

Mr. LAIRD. It is not generally known that this recommendation has been made by the new administration. I know that there are many medical schools throughout the United States that I am familiar with who feel that this section is very vital. And they would very much dislike to see it repealed this year. I was surprised that this recommendation came up here.

Dr. SHANNON. Well, sir, I might say that I feel that the most logical way to discuss the research facilities construction program is not necessarily the way it is proposed. I think that there should be matching, and I think there should be matching on a sliding scale. It is my deep conviction that there are very few schools in this country—there are very few vigorous research environments in this country—where, if one can provide attractive matching, the matching funds will not be forthcoming.

Now, when I am talking about matching, I am talking about matching 3 to 1; that is 25 percent by the schools, 75 percent by the Government or, we will not argue, 33 percent by the schools, 66 percent by the Government.

I feel that when one gets into general purpose laboratories, that the institution that is going to construct the laboratory must have the fiscal responsibility to conduct its program without complete dependence upon the Federal Government for total support—in other words, total support of the construction and total support of the program. I have a firm conviction that we need to have local involvement if we are to have realistic appraisal of needs.

I think in the special purpose programs, one has to have realistic matching. As I say, I think a 50–50 matching is too steep for some areas. The problem here is that one cannot syphon off a certain predetermined amount of institutional funds into a particular project that a particular investigator wishes to develop. At the present time institutions are scrapped for matching funds for education, broad education, as well as for scientific purposes.

But I think that if you have a wholly nonmatching program that does not relate to specific end objectives, you have a situation that may lead to the irresponsible development of facilities in the absence of any certainty that they will receive support over the long run.

Now, I think, quite frankly, Mr. Laird, that your program last year came closer to what I would say might be done on a nonmatching basis, because it is possible, in that program, in each case to identify, within a stable framework, a specific scientific objective and to compare the program objectives with the construction needs and to make a grant under one authority to do one and under another authority to do the other.

Mr. LAIRD. I thought it was important to have that program work through the individual Institutes.

Dr. SHANNON. Right. Well, I think to use that authority as a general construction authority is not very different from its extension to the centers program. That frankly provides construction funds for a specific program in which you take a specific objective and find out how much support funds they need and take the physical setup and decide how much construction funds they need. But when it comes to the broader issues of research facilities construction, then, I think, that the broad program requires one to have institutional involvement.

And as I say, sir, I am not convinced that, given a better match than 50–50—say, 25–75 or 33–66—I am not convinced from the inquiries we have made, that institutions cannot come up with that type of matching funds.

Mr. Laird. Of course, the program we had last year would not have been possible without section 433(a).

Dr. Shannon. That is right, sir.

Mr. Laird. And I would like to find out what your professional judgment is on this, and whether it was your recommendation that that be repealed.

NEED FOR AN INCREASED AND MORE FLEXIBLE CONSTRUCTION GRANT PROGRAM

Dr. Shannon. Well, I had two recommendations. One was that in the extension of our research facilities construction, the total sum be increased and that a flexible formula be adopted.

I was convinced that, if those two things could be achieved, we would not have an absolute need for a program such as was supported by the appropriation generated by your desires last year because, on balance, I feel that, while this type of general construction program would not satisfy all needs, it will satisfy most of the needs in the most responsible manner.

And I foresaw, frankly, Mr. Laird, the possibility, in the absence of a more favorable matching position, the possibility of a proliferation of independent, nonmatching programs, on the one hand, and a large 50–50 matched program, on the other, that, I think, would put our advisers and our operators in a position in which they could not really act in a responsible way.

I think if you have a basic program of one sort, you can always make an occasional exception and you can run a program. But if you begin to change the character of the basic program so that it is neither fish nor fowl, then I think you are in very deep trouble.

And it is my conviction, sir, as I say, that, given more favorable matching, that you can accomplish the bulk of the work. And I would say that one could probably accomplish the bulk of what will be done under the catchall program this year, although not all. As we cannot take a course satisfying every need, regardless of the cost, our problem—I mean administrative and accountability problems and all—is how to develop the best program that takes into account that our programs never will satisfy all the needs but will substantially satisfy the major needs and how to produce a situation that is conducive to our partners in the private groups doing their share.

I had a long talk with the group of physicians that came from Wisconsin. We talked about some of these problems. Incidentally, this was a very enjoyable session. This started off as a discussion of who should support the general practioner, who is just beginning to get involved in the research process. I thought this was a clear case where support for those fellows should have been derivable from local funds collected by the voluntary agencies. We went on to examine the role of the voluntary agency as the Federal programs develop further and further. I think that, if the local agencies within the State would become sufficiently knowledgeable about the needs for medical research in that State and could try to satisfy those needs and had a full appreciation of what can come from the Federal level, this mechanism could be brought to bear.

In other words, I do not believe that we have exhausted all mechanisms that are available to bring substantial funds from the private sector to the support of the programs. And I think that as the Federal budget gets larger and larger, unless we are very forceful in pursuing our objective and, in a solid way, find ways of bringing in the private section—this source of support will dry up. This is the worst thing that could happen in the medical research, if it became totally dependent upon the Federal Government for support.

So I think that some of my remarks in this particular context stem from these very long-term considerations, realizing that the program, as I propose it, will not do everything, but that, on balance and over the long haul, it is the peg that we are going to hang our hat on. This is a solid program that can be defended against all comers.

Now, I may be wrong, Mr. Laird, but these are my feelings.

THE UNIVERSITY OF CHICAGO

Mr. Laird. Are you dealing with the situation at the University of Chicago and their crying need for facilities?

Dr. Shannon. I am not at the present time. I was very well aware of the details about a year to a year and a half ago, when I went over the situation with Coggeshall, who was out there, and I know that it has gotten no better. At that time I do know that their construction program was so large in relation to their projected income, that Coggeshall did not know what he was going to do and did not see how he was going to evolve a program that could satisfy the need.

Mr. Laird. How is this new recommendation going to help out the University of Chicago?

Dr. Shannon. I think the one thing that is going to be of great help is the development of this new research facilities construction which, hopefully, will provide facilities both for undergraduate as well as for the graduate training.

Mr. Laird. That is a whole new program. Here you have this other authorization already in the statute. You do not have to come to Congress for additional legislation for a situation like this.

Dr. Shannon. I should point out that one of the main difficulties that Chicago finds itself in is that, in the absence of matching funds in the educational sector, they have to put a disproportionate amount of such fluid funds as are available to them into classrooms and the like, which automatically removes funds from research and research training. As you relieve the pressure for the more general program, then you make more accessible institutional funds for the research program.

But in the medical area the availability of attractive research funds—I am talking now about the research area—the availability of attractive matching funds, I am convinced, will not solve all the problems in a given year; but, given time, this could happen. Whether this would be suitable, I do not know. I would suggest——

Mr. Laird. Then you did not make the recommendations that formed the basis for this new bill that you have here before the Congress.

Dr. SHANNON. Well, you asked for my personal judgment. The bill before the Congress is for 50–50 matching.

Mr. LAIRD. That is correct. And I thought that this determination you were talking about and your reason for recommending the repeal of section 433(a) was that you were going to have a sliding scale.

Dr. SHANNON. I said that our recommendations for the new bill encompassed two things—one, a sliding scale; and, two, the larger dollar amount.

Now, the larger dollar amount part of that was bought, but the sliding scale was not.

Mr. LAIRD. Now, does that change your opinion on section 433(a)?

Dr. SHANNON. I think there is going to be, from what I can gather, sufficient pressure in the outside groups who are facing the harsh realities of construction, that there are going to be very large presentations to the Congress to provide more favorable matching in the research facilities construction area. And I hope that when the bill comes out of the Congress, it will provide more liberal matching than is now proposed.

Now, I would be willing to gamble on that. And I think that, if they cannot obtain more favorable matching, then I think that you would have a fair proportion of supporters for your view, in the absence of more favorable matching, there should be no repeal of 433(a).

Mr. LAIRD. I think you are going to find a lot of opposition to the administration position to go ahead with only a 50–50 matching program and eliminate section 433(a).

Dr. SHANNON. If the present bill is enacted as such, I think there is going to be a serious deficiency because I think that many schools cannot develop the research plans they desire on a 50–50 basis.

But when one discusses how one is going to modify one's position in relation to 433(a), that presupposes the passage of the present bill as it stands. I would rather hope that the present bill will be modified by the Congress to provide a sliding scale with more reasonable matching, depending upon a series of factors that I think are definable. And this is the outcome that I, if I were an outsider subject to the same pressures that I now have, would work for.

Mr. LAIRD. Who is to make the recommendation that a school should get $2 for every dollar it puts up or $1 for every dollar it puts up? What is the difference between that determination and the problem that you have with section 433(a) and the present Research Facility Act?

Dr. SHANNON. Well, the difference between the two is, at the very least, that if there is some participation on the part of the institution, you can be sure that the institution is unwilling to put a substantial number of hard dollars on the line unless they have assured themselves that they have the stability to run the operation. In other words, they will not be "blue-skying" in the construction field, where the program is a big program, but will develop a very realistic program based on both the availability of scientists and a solid program of research.

The main difference between matching and no matching, in the general construction area, I think, will be the presence of very hard-thought-out programs, as opposed to a mixture of programs, some of which will be very thoughtfully prepared and others which will be just wishful thinking.

And I would think that we are in such a difficult position sitting at the Federal level trying to develop—when I say "we," I mean our advisers; and, for that matter, the Director of NIH and the Surgeon General, who, in the final analysis, has to sign the grant—in such a difficult position in trying to develop a concept of what is wished for out of a piece of paper—even aided by site visits—that we would like to feel, at the very least, that the Institute is joining with us. I would just like the Institute to speculate with us, rather than just asking us to speculate alone.

Mr. Laird. It seems to me that, with the need for facilities being so great, there is an area here in the individual institutes where they could use to advantage funds for the construction of facilities on a categorical basis throughout the United States. This seems to me to be the thing that we lack the most as we face the next few years.

Dr. Shannon. Yes, sir. And there I am in no small amount of contradiction myself, Mr. Laird. I agree with you completely that there are areas of science in this country where the program can be highly, specifically defined, where the construction need is clear—where the institution has already made the commitment, and where a solid program is assured.

But I would point out that the difficulty that I find myself in, in trying to evolve the guidelines for a broad construction program for the Nation, is the realization that there are only unique areas in science where this is possible, and——

RESPONSIBILITY FOR RECOMMENDING REPEAL OF SECTION 433 (A)

Mr. Laird. That is why I ask you for your own personal opinion and your best judgment as to whether that section should be repealed from the Public Health Service Act.

Dr. Shannon. Well, if you ask it in that way, I would say, "No, sir."

Mr. Laird. How do you feel about it, Dr. Terry?

Dr. Terry. As a matter of fact, Mr. Laird, I am not even certain what you mean by repeal of 433(a). I am not even aware that such a recommendation has been made.

Mr. Laird. Well, the President sent up a message a week or so ago in which he included a bill to extend the Health Research Facilities Act.

Dr. Terry. Yes.

Mr. Laird. On a 50–50 basis.

Dr. Terry. Yes, sir.

Mr. Laird. But in his recommended legislation he included a section to repeal 433(a) of the Public Health Service Act. That is what I was addressing myself to. That particular section gave to the Public Health Service the authority to construct research facilities on a nonmatching basis if there was a need for it.

Dr. Terry. Yes, sir.

Mr. Laird. And in this new recommendation that we have from the President, that particular section is recommended for repeal.

Dr. Shannon. I would like to extend my comments to say that in its place was a section that proposed authority to construct on a national basis those facilities that were of regional or national importance.

Mr. LAIRD. Well, this was the way to save these primate colonies. You sort of pulled section 433(a) out of a hat a few years ago and revitalized it to build facilities for these primate colonies.

I was pretty disapponited when the new administration recommended repeal of section 433(a). I really think that they should have at least informed you as the Surgeon General that they were making such a recommendation, and perhaps even go so far as ask your opinion.

Dr. TERRY. I should have known it was in here, and I do not know how I overlooked that particular feature.

Dr. SHANNON. Well, I would just like to comment on one thing. This is not germane—it is a clarifying comment.

NEED FOR REGIONAL OR NATIONAL CENTERS

The need for regional or national resource centers is a need that we have felt has existed for many years. For instance, the lack of authority to construct such a series of facilities almost wrecked the cancer chemotherapy program before it got off the ground, because there was not present in this country a sufficient number of installations to raise the hybrid animals that were required to conduct a program.

Now, had we been able to take care of this, we would not have come to the Congress with a request to include the establishment of such a unit in a contract with a university or nonprofit organization or the like. We are now in the position, in the cancer diagnostic program or the viral program in cancer, of needing to have produced large quantities of specific antiserum quite like fungi or viruses. It is not commercially available, nor will it be made commercially available until a large operation is developed. It will have to be developed, I think, in the course of the next year or two. We will require it for the development of a disease-oriented program in the universities. We will plan for manufacturing laboratories to produce these things. Again, we encounter here the inadequate supply in this country of hybrid animals for a variety of purposes.

So this authority to do construction for such a purpose and to operate a facility by contract or otherwise, is a broad need that will stand, Mr. Laird, on its own feet. In other words, I do not think it is an "either-or," but in the absence of 433(a) authority, this cannot be done at all.

NECESSITY FOR CONTINUING USE OF AUTHORITY UNDER SECTION 433(a)

Mr. LAIRD. Well, I just want to make it clear here that there has been a lot of misinformation put out about this use of section 433(a) in this bill last year. I would not have been for the use of this section in that legislation if it was a one-shot proposition for one particular institute. This has got to be a continuing proposition in order for it to do any substantial good.

Dr. SHANNON. Well, as was explained to the committee before, our interpretation of the legislative history of the appropriation, however erroneous it may be as we read the record, was that this was a one-shot program.

Mr. LAIRD. It is no more a one-shot proposition than any other section of your budget.

Dr. SHANNON. No, Mr. Laird, I say this——

Mr. LAIRD. Because the Congress each year reviews the budget, and can cut off any part of the program through failure to appropriate for any section of the Public Health Service Act. Now, a majority of the Congress may at any time come to the decision to cut this program out or cut that program out. But that is a decision that has to be made in the yearly review of the budget. That cannot be a decision that is made in advance.

Dr. SHANNON. Well, we interpreted the appropriation, as I say, at this point erroneously.

But, historically, our interpretation was that there had been an agreement in conference that this is not a program that the committee would be reactivating in years to come.

Mr. LAIRD. The conference never agreed to that. This idea of making a determination in advance of the action on the 1962 budget makes me wonder a little bit.

And then when I see this message from the new administration—and I only saw it this weekend, or I would have been questioning the Secretary of Health, Education, and Welfare on this particular matter. But the legislation was not made available to me until, I guess it was Friday.

Dr. SHANNON. It was very recently submitted, was it not?

Mr. KELLY. I do not remember when.

Mr. LAIRD. I do not even believe the Secretary understands section 433(a) is recommended for repeal, because he sat across from me at this table, and I discussed this matter with him, and he did not indicate in any way that he was recommending the repeal of that section.

Dr. SHANNON. I think our error, quite frankly, is that, having assumed that this was the position regarding 1962, we should have formally requested an opinion from both the Appropriations Committee of the House and the Appropriations Committee of the Senate whether there was any uncertainty as to what was in fact the intent of the funds made available. We did not do that, and I think that, had we done this, our program this year would not have been particularly different in terms of any grants that we made available. But our position for the years ahead would have been quite different.

CLINICAL RESEARCH CENTERS FACILITY MODIFICATION

Mr. LAIRD. This morning we discussed the clinical centers and it seems to me that this has developed into a program that is a little different than the understanding that I had of it when we appropriated the funds. It seems that the major portion of the funds that you are allocating this year are in the area of modifying certain space in hospitals to provide the facilities to carry out programs in the future.

Is that correct?

Dr. SHANNON. Not entirely, sir. During the initial months, the funds would be expended that way, but these programs will operate within 3 to 4 months after they are begun, and part of the reason for the slow start will be the acquisition of staff and development of teams of researchers. They will have an ongoing program well within the initial year.

I do not want to create the impression that all of the funds in the first year are primarily for rehabilitation or renovation, but, rather, that in this program the major part—and in many cases, up to about 50 percent—of the first year's funds and up to, I would say, perhaps 3 or 4 months of the first year's operation would be devoted to getting a facility in operation.

Mr. LAIRD. You say this is 50 percent, approximately?

Dr. SHANNON. Approximately, I think that is what it would average.

And all these programs would be well underway 6 months after they are initiated, but we will not be under full steam, I would guess, before the end of the year; and no small problem will be the acquisition of personnel.

Mr. LAIRD. When I talked to Dr. Farber about this program—he was one of those that was interested in it at a very early time—he indicated to me that the idea was to rent hospital beds as far as the cancer research was concerned. He said that there were certain people that they wanted to keep in the hospital for a longer period of time, and that they would be able to take 15 or 20 beds in a particular hospital and study these patients over this longer period. I did not realize at that time that the idea was to remodel, or whatever term you want to use, facilities.

Dr. SHANNON. Well, Dr. Farber, looking at his own institution, had as his primary need for his own research program the support of beds that are already in being. In Children's Hospital he has a very good laboratory setup that is closely adjacent to facilities for the patients. And the primary need in his case is, in fact, bed support; and in certain of our clinical research centers this is also the case.

But, on balance, I think that the bulk of the centers will require some space adjustment, more particularly so as to provide observational facilities for a small number of patients in partial isolation and the development of laboratories immediately adjacent to the patient areas, to carry on the techniques.

Now, in our minds, the concept as initially proposed has not changed. We are trying to carry through on the basic concept that was initially expressed some 2 years ago.

Mr. LAIRD. Well, these discussions were held probably 3 years ago.

Dr. SHANNON. Well, the thing that is confusing here is that during the initial year when these units were authorized by the Congress, there were two different proposals. One related to heart and the other related to cancer. It was in discussions, although not as an outright proposal, that the need for general facilities was brought out—in fact, in our testimony. Now, the original proposal that was made——

Mr. LAIRD. Well, can we keep on cancer research now? I would like to talk about heart a little later.

Cancer clinical facilities must be a little different than the heart facilities.

Dr. SHANNON. Yes, sir, they are.

Mr. LAIRD. In cancer you are going beyond the idea of just providing beds?

HISTORY OF CLINICAL CENTER APPROPRIATION

Dr. SHANNON. Yes, sir. But I have to get to that. It takes a cycle of a year, because the original support for the cancer centers was given by Dr. Farber, and ended up with a program of about $20 million. And the Senate, in putting these funds in, decided they would start with a much smaller amount and in a noncategorical area, rather than a highly specialized area. What they did was put $500,000 in each of six Institutes to emphasize the multicategorical nature of the work to be done with these beds, and instructed us to bring those appropriations—this was $3 million—to a central point for administration and to establish the more general type unit as a beginning.

Mr. LAIRD. Where was that?

Dr. SHANNON. That was in the Senate report, sir.

Mr. LAIRD. But that was not agreed to in conference.

Mr. KELLY. No, I think it would be in the Senate report with respect to their recommendation for a larger sum of money.

Mr. LAIRD. Dr. Shannon, I do not believe that was in the report of the conferees after we apportioned $500,000 out to each one of the Institutes. I believe that that was thrown out in the conference.

Dr. SHANNON. The apportionment of $500,000 to the Institute came after the Senate report.

Mr. LAIRD. It did. And that did away with the idea that the Senate had of taking this out and having it administered in one place. The conferees agreed to put it in the individual Institutes. We appropriated the money to the individual Institutes, and I think that the conference report clearly shows that.

Dr. SHANNON. Well, sir, I cannot argue that. I do not recall. But I would say that one of the——

Mr. LAIRD. You were talking about language that was in the Senate report prior to the conference, before we appropriated it to the Institutes?

Dr. SHANNON. My guess is that there were probably very little in the way of instructions in the conference report, Mr. Laird.

Mr. LAIRD. Except that we did make the appropriation direct to the individual Institute.

Dr. SHANNON. This is correct. And again I suspect, although I have to check on the history of this, that we took the presentation as it was made on the floor—this is my best recollection—by the Senate in presenting the appropriation, and we felt secure in doing that because the initial proposals for these funds originated in the Senate appropriation. We followed that instruction as best we could, because there was no doubt in our minds——

Mr. LAIRD. Well, it seems to me, Dr. Shannon, that the thing that is guiding the National Institutes of Health in their operations and administration of programs in many of these cases are the statements that are made on the floor of the Senate.

Dr. SHANNON. It could well have the effect of doing it, sir.

Mr. LAIRD. Well, it seems to me that, as far as setting up these clinical centers, that the Cancer Council and the Heart Council should be in a position where their recommendations are given considerable weight.

Dr. SHANNON. Then I would move to the following year, when funds were made available in both heart and cancer, but in additional and smaller amounts, in mental health and neurology.

Now, these funds will be expended wholly at the direction of those councils and will not be centralized. The expansion of the general program is proposed in the Division of General Medical Sciences, not as a distributed item.

Now, in the case of both the heart and cancer, we have insisted that the administrative arrangements be handled separately and computed separately for these quite expensive facilities in which one is dealing less with the scientists than the hospital administrators; but that, if they chose in addition, to make parallel grants both for the support of beds and for the support of the program that would be performed in those beds, this was wholly within the responsibility of the respective council to determine.

So that this year you will see action by the Division of General Medical Sciences that relates purely to the resource while the program for those resources is taken up by the individual institutes—in some cases two or three, in other cases all the institutes.

In heart and cancer, mental health and neurology, where no action has yet been taken on any of the programs but will be discussed and acted on definitively in April, you will find two types of actions. The first type of action will be to provide a resource, where they feel that the funds in support of the program of an institution is already adequate they fully occupy the resource they propose to furnish. In other cases they will provide the resource, which will be the clinical area, and its full support and, in addition, an expansion of grant funds to enable the institution to utilize the resource fully.

Now, how these will come out I could not tell you at the present time, although I suspect that in the case of the Cancer Council—well, I would rather not guess, because they have not been presented with the development of staff work which is still underway. Project activities have not been considered, and the special committees that will consider this have not met. So I would rather not prejudge the recommendations of the Councils.

Mr. LAIRD. It is getting late. I have quite a few questions about this statement, but I am going to try to cover them as rapidly as possible.

PROPOSED INSTITUTE FOR CHILD HEALTH AND HUMAN DEVELOPMENT

I notice that your statement strongly supports the President's initiative in requesting Congress to authorize a new National Institute for Child Health and Human Development.

Dr. SHANNON. Yes.

Mr. LAIRD. It does not go into this in much detail. Do you propose that under this new Institute, if it is authorized, that you will separate from the Heart Institute and Cancer Institute and all other institutes, the work they are doing on the problems facing the child, and make them the responsibility of this new Institute?

Dr. SHANNON. We will separate some of the problems, should this Institute come into being.

But to give you some dollar figure, since you are trying to determine a magnitude, we calculate that roughly $25 million of grants are presently being made in support of the general activities that could be related to the new Institute. It is our estimate at the present time that only $5 million of the $25 million would be suitable for centralization. We would possibly take the position that those studies which primarily center around disease orientation or disease entity or groups of diseases that have more relevance to the disease itself than to the developing child should be reached in the disease oriented categorical institute.

Mr. LAIRD. Do you think it would be of any value to set up an institute for the aged?

Dr. SHANNON. No, sir. I think that, although it seems a little bit peculiar, at first blush, to join the child with the aged in a single institute, that this has a very solid basis. I think they will go very well together. All the experimental work will use the time scale as the independent variable. They will be concerned with total life studies in the experimental field, rather than cross-sectional studies, as is more common in the disease-oriented categories. They will be much more concerned with the environment which has a more profound influence on the developing child and a more profound influence on the aged than do the peculiar diseases to which they are susceptible.

Mr. LAIRD. Where will research on rheumatic heart disease be?

Dr. SHANNON. That will be in the Heart Institute.

Mr. LAIRD. That will be in the Heart Institute?

Dr. SHANNON. Yes, sir.

Mr. LAIRD. You do not intend to take away anything, then, from the various categorical institutes?

Dr. SHANNON. Yes, sir; we will. We think that some of the basic programs in the behavioral sciences that have impact on the understanding of the developing child, where one is concerned with the development of excellence as well as the development of retardation, should be in a separate category. Certain aspects can be better studied in relation to total development than in a disease-oriented environment. We feel that those relationships, or those factors, which are heavy components in the emotional development of the child, quite apart from disease or disease orientation, warrant separate study.

Mr. LAIRD. You would take those away from the Institute of Mental Health?

Dr. SHANNON. Well, in fact, they are not doing too much at the present time.

This is an area that gets a bit thin when it comes to our authorization to make studies that are, frankly, in behavioral areas.

Mr. LAIRD. Why do we not divide up the work of the National Institutes of Health along a little different line then? Why do we not set up an institute for the child and one for the middle-aged and one for the aged and get away from this disease approach we have now?

Dr. SHANNON. This is a logical approach. Historically, it would be difficult to do at this time, but I can see no conflict or any cause for concern or trouble in the program that you propose. There are certain fundamental studies, for instance, in aging, that have required the setting up of a center to attempt some correlation of the various activities, to provide some focal point where they will be brought together, where they can be assessed, where new programs can be stimulated. We feel that there are comparable deficiencies in our studies of the developing child. But we feel in both cases that the behavioral aspects are sufficiently related to the disease as such, that this should be a consideration and a responsibility that goes beyond a straightforward disease-oriented program.

Actually what you see emerging here is an area of concern relative to health that has not received much attention in the past, in pretty much the same way that we are now beginning, for the first time, to pay serious attention to environmental hazards of a chemical nature and the like, that are the basis for the establishment of a Bureau of Environmental Health.

Now, here again, there are many areas of environmental health that have impact on the categorical programs. The environment as a source of chemical agents in cancer causation, for example. But we feel that for the Cancer Institute to extend its concern from the genesis of cancer to a more general consideration of the environment, and all of the things that may be health hazards in the development of technology, is not wise.

POSSIBLE ROLE OF CHILDREN'S BUREAU

In a somewhat similar sense, we look at the problems of the child, and we feel, quite frankly that attention to the emotional development of the child, without regard to overt disease, probably would pay more dividends than serial studies of such specific problems as juvenile delinquency.

Mr. Laird. Why cannot this be done by the Children's Bureau?

Dr. Shannon. This is as much fundamental research as is fundamental research in any other areas. I do not think the Children's Bureau is set up or organized, or traditionally has shown the competence to undertake a broad program of this seriousness.

Mr. Laird. They would like to. They have been saying for some time that they feel they are set up to carry on a research program. It seems to me that we are getting the National Institutes of Health a little confused here with work that really belongs some place else. Part of this description that you have given me, I believe, should be the responsibility of the Children's Bureau.

Dr. Shannon. Well, sir; the Children's Bureau have traditionally been responsible for carrying out a series of programs that are not dissimilar to many programs that are a characteristic of the Public Health Service through the Bureau of State Services. Quite frankly, I would feel that the most important thing is that fundamental studies of the nature that I have described should be established in the context of the total medical research program, because they will be inadequate without very broad support of this nature.

Now, if it is the will of Congress that this be done in the Children's Bureau, rather than NIH, I think the important thing is that it be done, and that it be done well.

Mr. Laird. They have authorization, you know, to do this kind of work.

Dr. Shannon. I believe that they have very broad authorization. But, traditionally, as I say, they have been concerned with technical assistance and grant programs and things of this sort; whereas we have been primarily concerned with an equally broad segment of this problem from the fundamental science side. And I quite frankly think that it is easier for us to spread our umbrella to encompass this area than it is for the Children's Bureau. But this may be a difference of opinion.

CHILD HEALTH CENTER

Mr. LAIRD. In your statement you make reference to the establishment of the Child Health Center. Where do you get the money to establish this center?

Dr. SHANNON. Well, the cost of the center today is zero.

Mr. LAIRD. What is this center doing that it is not costing you anything? It is an interesting phenomenon in government.

Dr. SHANNON. We have established the organization, but we have not recruited the person to head it. Until we find the person to head it, we will not have an active organism. Now, these funds at the present time come out of the general planning funds that are available to the Division of General Medical Sciences. This is a part of total planning of NIH; whether we have an institute or not, we have a very broad commitment for research and training in the areas that would be encompassed by this, and we feel that this type of center, like the Center on Aging, is a very worthwhile expenditure of funds.

Mr. LAIRD. What is in the 1962 budget for the Child Health Center?

Dr. SHANNON. I do not believe there is anything.

Mr. LAIRD. Are you going to operate this next year for zero too?

Dr. SHANNON. No. We will operate between now and the end of the year out of funds that are available for program planning, in Dr. Hunt's position or mine. And by the end of the year I think we will have a very good idea as to whether we will or will not have the broad function.

Mr. LAIRD. How many other programs of the National Institutes of Health could we finance this way?

Dr. SHANNON. This is going to cost you money before you finish.

Mr. LAIRD. But there is no estimate before us.

Dr. SHANNON. No, sir. We have a proposal for the technical contents of the legislative proposal that Dr. Terry has just seen for the first time as of yesterday; we hope, before the end of this fiscal year that it will be clearly apparent whether we will or will not be performing the function.

Mr. LAIRD. There has been quite a little publicity about the establishment of a Child Health Center, and now I asked a few questions about it and I find that there is not one.

Dr. SHANNON. Well, there is and there is not.

Mr. LAIRD. This has been handled very well by the public relations people. They have got the country believing that there is a big new program, and now I find that it is costing zero and it is doing nothing.

Dr. SHANNON. There has been a great deal of staff work on the study of what our program contains at the present time, what it should contain when the center is evolved. But this is a pickup staff that is not charged to the center as such. These personnel have come from the Office of Program Planning, in the Office of the Director of the NIH, the Division of Research Grants, and Dr. Hunt's Division of General Medical Sciences.

I do not want to create the impression that, having created an office, we have not moved in this area simply for lack of the chief of that office. We have moved a great deal in our analyses of programs, and we are now in program development for this Institute.

I think that this work will be valuable to us, whether the Institute is or is not established or, if it is established, whether it is established at the NIH or the Children's Bureau.

I would say that, if the Institute is authorized at this point in time, most certainly we will ask in the authorizing legislation for the ability to apply for funds. And there will follow, if it has the concurrence of the Department and of the Bureau of the Budget, a supplemental request for funds.

But in the light of the present legislative status of the Institute, we do not feel that we should provide in next year's budget for any funds for this.

Mr. Kelly suggests that we should give you for the record how we have developed the information on the Child Health Center, the devices we have used to develop the information we have.

Mr. Laird. If you come out with a figure of zero, I am going to be quite amazed.

Mr. Kelly. No, it will not, Mr. Laird. We will submit for you how, out of the funds recommended for 1962, we will fund the center, and what its costs will be.

Mr. Laird. Well, Mr. Chairman, I think I can cover the rest of my questions with the various institutes as they come up.

Mr. Fogarty. Thank you very much, Dr. Shannon and Dr. Hunt.

Highlights of Progress in Research at Clinical Center, 1960

We will place the usual highlight statements, of other than categorical institute research in the record at this point.

(The statements referred to follow:)

Items of Interest on Program Developments and Research Studies Conducted and Supported by the Clinical Center

PHYSIOLOGICAL MONITORING SYSTEM FOR CRITICALLY ILL PATIENTS

In keeping with its mission of originating new hospital methods, the staff of the clinical center has developed an electronic device for monitoring the physiological functions of postoperative and acutely ill patients. Help with technical details and production of the finished product was obtained from Gulton Industries, Inc., Metuchen, N.J. It was financed by the National Cancer Institute.

Development of new medical and surgical techniques, plus common use of ever more potent drugs, has greatly increased the nursing time required for such patients. It is no longer unusual to find a patient requiring two special nurses to supply the intensive care needed postoperatively. The time of one of these nurses is taken up almost exclusively in frequent recording of vital signs.

Space medicine techniques for measuring certain of the vital functions have been adapted to clinical use. It was decided that the five signs most needed in following an acutely ill patient's condition are (1) blood pressure, (2) pulse, (3) temperature, (4) respiration, (5) arterial oxygen saturation.

To be of value, the monitoring system had to have an alarm which would indicate which function in which patient had exceeded the tolerable range set for that patient. It had to have some type of visual record to indicate the values received into the equipment from the patient. It had to be simple in its operation so that it would not require a highly skilled technician in its use. It had to have a "fail safe" system which would indicate when the unit itself was not functioning properly. Lastly, it had to be small enough to fit into the patient's room. It was also determined that to be practical the system should monitor four patients, the number of beds available in the largest recovery room in the clinical center. The device was installed late in the month of November.

A great value of the physiological monitor is that it records all measurements taken. A "print out" is part of the equipment and it gives a permanent written record in alpha-numerical form for each patient at whatever interval is determined to be necessary. The form may be pasted directly into the nurse's notes on the patient's chart and thus saves the time necessary for transcribing.

It is stressed that the Clinical Center does not feel this system will, in any way, reduce nursing hours necessary for the care of patients. It is an auxiliary aid for the nurse which allows her to perform the functions that only a nurse can perform, but it should make for better and more efficient patient care.

RADIOPHARMACEUTICAL SERVICE

Until this year radioactive drug products used at the Clinical Center were prepared by individual investigators or were received from manufacturers. Sometimes the manufactured product was not entirely suitable to the particular need of the investigator. To keep in step with the ever-growing demand for this type of pharmaceutical, and to give investigators more time to devote to their primary function, a Radiopharmaceutical Service has been established.

For the most part, investigational-type radioactive drug forms are prepared by this Service for diagnostic use, but it also compounds some few oral drugs for treatment in dosage forms. Preparation of these products is governed by the same controls and accuracy as all other drugs available in the Pharmacy Department of the Clinical Center. They are given safety tests for pyrogenicity, sterility, and radioactive assay. The latter test is performed by the Radiation Safety Office.

In cooperation with clinicians and laboratory investigators, radioactive drug products which are not available from any other source are developed and synthesized. Examples are the development of chromium 51 labeled human serum albumin; I 131 labeled gamma globulin; oral fat emulsion with 131; and improvement of previously developed polyvinyl pyrrolidone—I 131 injection, and krypton 85 injection. The Radiopharmaceutical Service cooperates with industry in working toward a safer, purer product for patients. This is a mutually beneficial arrangement in which information is freely passed back and forth since all knowledge gained is to mutual advantage and serves the general cause of research.

AUTOMATION IN CLINICAL PATHOLOGY DEPARTMENT

Laboratory consultation and services for patient care are provided to the Clinical Center by its Clinical Pathology Department in the fields of clinical chemistry, hematology, microbiology, and special diagnostic procedures. Because of the research mission of the Clinical Center, laboratory tests for patients participating in research projects are far greater in number and variation, with more exacting quality control, than those required for care of patients in general hospitals.

The Department has continued to improve the efficiency of current tests and to introduce new procedures which will be helpful to the clinical staff in patient care and clinical research. For example, the use of automatic instrumentation in this Department has proceeded at a rapid pace.

The Hematology Service has developed an automatic attachment for the modified Coulter electronic cell counter which was installed last year. This attachment enables the technician to obtain size distribution curves of red cells in seconds, and provides an accurate automatic technique for counting platelets. Although experimentation with the device is still in progress, it is being used now on a limited number of studies such as blood analyses for certain leukemia projects.

In the Clinical Chemistry Section, measurements of blood glucose and blood urea nitrogen, serum phosphatase, and serum bicarbonate are now being determined routinely by the autoanalyzer. Many of the other routine chemical estimations are performed partially on an automatic basis. Examples of these tests are measurements of phosphatase, creatinine, total protein, and albumin. All of these procedures employ a systematic method for the measurement of samples and reagents and are read on a semiautomatic recording photometer.

Active programs are in progress to automate the flame photometer of serum cations, including sodium phosphatase and calcium.

HIGHLIGHTS OF PROGRESS IN RESEARCH ON BIOLOGICS 1960

ITEMS OF INTERST ON PROGRAM DEVELOPMENTS AND RESEARCH STUDIES CONDUCTED BY THE DIVISION OF BIOLOGICS STANDARDS

The Division of Biologics Standards administers those provisions of the Public Health Service Act pertaining to the control of biological products in interstate and foreign commerce. Two types of licenses—establishment and product—are issued for the production and sale of such products, following a determination by the Division that the prescribed standards for safety, purity, and potency have been met. In the first 11 months of the calendar year, 188 establishment licenses and 278 product licenses were in effect, the latter covering 1,228 specific products. Tests of approximately 8,000 individual lots of various biological products were made, ranging from relatively simple sterility tests to potency determinations involving both animal and tissue culture tests.

Of equal importance in insuring the continued safety, purity, and potency of these products is the preparation and distribution of physical reference standards to manufacturers and laboratories engaged in biological standardization throughout the world. Approximately 4,000 vials of such standard preparations are distributed each year by the Division.

The Division's research is a vital part of its program. Continuous efforts are made to improve and to develop new testing procedures, as well as to improve methods of preserving and storing physical reference standards, to correlate them with standards established in other countries, and to develop new ones.

RESEARCH STUDIES

Characterization of attenuated polioviruses in the oral vaccine and after passage in man

The most recent findings in continuing studies of the properties of attenuated poliovirus strains, and the characteristics of these strains before and after gastrointestinal passage in man, were reported by Drs. Ruth Kirschstein and Samuel Baron, Laboratory of Viral Immunology, at the second International Conference on Live Poliovirus Vaccines.

Low neurovirulence for monkeys is considered a prerequisite for virus strains to be used in live poliovirus vaccines—the proposed strains were selected on this basis. A comparison of the neurovirulence of the attenuated poliovirus vaccine strains, when inoculated directly into the central nervous system, was reported last year.

Current studies show that some attenuated virus strains retain their ability to invade the central nervous system of monkeys when inoculated intramuscularly. This was demonstrated by histologic lesions in sections of the brain and spinal cord and by paralysis of some monkeys. Two routes of spread from the site of inoculation to the CNS appeared to be possible—either through the bloodstream or along the peripheral nerves. It was concluded that the nerve supply of the inoculated muscle was the only way it could be prevented.

An additional requisite for virus strains to be used in live poliovirus vaccines is stability of low neurovirulence characteristics during vaccine production and human passage.

The results of these continuing studies indicate that (1) the temperature character as determined in a plaque system is very often correlated with monkey neurovirulence; (2) minor laboratory manipulation of the vaccine strains often results in marked alteration of the virulence characteristics; (3) virus obtained from stool examinations of persons fed vaccine virus exhibited a high frequency of increased monkey neurovirulence.

Results of these studies have been applied as additional criteria for selection of strains for oral vaccines.

Poliovirus inhibitor found in rhesus monkey central nervous system

During studies in which rhesus monkeys were inoculated intracerebrally and intraspinally with attenuated poliovirus—an established neurovirulence testing procedure—an unexpectedly low rate of virus isolation from the central nervous system (CNS) of the infected monkeys was observed. Moreover, when infected CNS tissue was plaque-assayed on monkey kidney cell cultures, more virus plaques appeared at higher dilutions of CNS tissue than at lower dilutions, strongly indicating virus inhibition.

In a study undertaken to determine the nature of this phenomenon, Dr. Samuel Baron and coworkers, Laboratory of Viral Immunology, found that the inhibition was not directed against virus but affected viral multiplication by altering the host cell (Science).

When suspensions of lumbar or cervical cord tissue were assayed for poliovirus content, virus was recovered from only 30 percent of the infected monkeys, whereas in previous studies, recovery of virus from CNS tissue of infected monkeys was readily obtained. Further tests revealed that suspensions of CNS tissue could inhibit up to 900 plaque-forming units of poliovirus in cell culture. Moreover, the inhibitor was found in the CNS suspensions of normal as well as infected monkeys.

Although the inhibitory effect of monkey tissue was demonstrated against each of the three types of poliovirus, no significant inhibition of Coxsackie A9 and Echo 12 viruses could be demonstrated. This indicates some degree of specificity of the inhibition. Furthermore, when the CNS tissue suspensions were combined with large amounts of poliovirus and then diluted for plaque assay, no inhibition was demonstrated, indicating that the inhibition did not irreversibly neutralize the virus, but in some way affected viral multiplication by acting on the host cells.

Neurovirulence of type 1 poliovirus carried by ribonucleic acid (RNA)

Previous studies by several investigators have shown that the ribonucleic acid (RNA) of a number of animal viruses, when extracted from the virus particle, will initiate infection in tissue cell cultures. Although these studies indicate that the infectivity is due to the RNA itself and not to residual virus particles, it was not known whether subtle differences in the genetic makeup of the virus could be transmitted by the RNA. On such difference would be the virulence of the virus particles for animals.

Drs. Paul Gerber and Ruth Kirschstein, Laboratory of Viral Immunology, have presented evidence that genetic information controlling neurovirulence and other characteristics as well as infectivity, are transmitted by the viral RNA (Journal of Experimental Medicine).

The study was made with two type 1 poliovirus strains which have been adapted to mice by Dr. C. P. Li. Laboratory of Virology and Rickettsiology. The LSa strain is virulent for mice; the LSc strain is an avirulent variant developed from the LSa strain. Although the RNA from each strain had the same infectivity for cell cultures, the RNA from the virulent strain was highly neurotropic for mice when inoculated intraspinally, whereas the RNA from the attenuated strain was completely avirulent for mice.

Additional evidence that the inheritable character of virulence was maintained following passage of viral RNA was derived from an experiment with rabbit kidney cell cultures infected with LSc-RNA and LSa-RNA.

Although intact poliovirus cannot infect rabbit kidney cells, it was possible to induce limited infection with the isolated RNA. The viral progeny from such infected cells, when inoculated intraspinally into mice, produced infections characteristic of the parent RNA virus.

Moreover, when the progeny of the Mahoney-RNA in monkey kidney cell cultures were incubated at 40° C., their reproductive capacity (*t* marker) remained undiminished. In contrast, the RNA extracted from the highly attenuated LSc virus failed to synthesize complete virus at that temperature.

Cell cultures found to develop resistance to photodynamic action

During studies of poliovirus by plaque assay technique, workers observed that the top layer of monkey kidney culture would frequently degenerate within 48 hours after application of overlay medium. Since this raised a problem in interpretation of viral assays, a study was undertaken to determine the cause of this degeneration.

Experiments were conducted to determine the variables of temperature, dye, and light. The results indicated that the combination of neutral red dye and light was the damaging factor. However, when cells stained with neutral red were incubated in the dark overnight, cell degeneration did not occur following exposure to light. Although other workers have described the occurrence of photodynamic action on cells, development of resistance to photodynamic action has not been reported previously.

From a practical point of view, the discovery makes possible the elimination of unexpected cell degeneration during virus assay by shielding the infected cell cultures from light during the initial 12 to 16 hours of the 6-day incubation period.

Of academic interest is the mechanism by which cell resistance developed. There were two possibilities: the resistance could be due to a change in the cells or to alteration of the dye. Cultures which had developed resistance to light after incubation with neutral red for 48 hours were also found to be resistant to sensitizing action of the addition of fresh dye. This indicated that loss of sensitization was probably due to a change in the cells rather than alteration of the absorbed neutral red. Furthermore, when neutral red was extracted from resistant cell cultures and applied to fresh cells, the cell cultures died after exposure to light, indicating that there was no alteration in the dye.

A complete report of this work, coauthored by Alice M. Gochenour and Samuel Baron, Laboratory of Viral Immunology, appeared in the Proceedings of the Society for Experimental Biology and Medicine.

Ineffective nucleic acid (DNA) isolated from polyoma virus

The first evidence that an isolated nucleic acid will turn a normal cell into a cancerous cell has been reported by Sloan-Kettering Institute and NIH scientists.

Preliminary work on the isolation of infectious deoxyribonucleic acid from SE polyoma-infected tissue cultures was published early this year in the Proceedings of the National Academy of Sciences by Drs. G. A. Di Mayorca, Sloan-Kettering Institute; Bernice Eddy, DBS; Sarah Stewart, NCI; et al. (The SE polyoma virus, originally isolated from leukemic mice by Drs. Stewart and Eddy several years ago, has to date produced more than 20 types of tumors in a number of species of laboratory animals.)

Isolation of infectious nucleic acids, either from purified viruses or virus-infected animal or plant tissue, have been reported by various workers, with positive identification of RNA as the infectious agent, but no well-substantiated findings of DNA. The induction of tumors in mice with preparations of mixed nucleic acids from leukemic mice also has not been clarified (Hayes and Latarjet).

The most convincing evidence for the successful isolation of an infectious nucleic acid depends on its sensitivity to a specific nuclease. The authors report the isolation from mouse embryo cultures infected with SE polyoma virus of an infectious nucleic acid which is resistant to the action of ribonuclease (RNase) but which is destroyed by deoxyribonuclease (DNase). The intact polyoma virus is resistant to both enzymes.

The virus was grown in mouse embryo cells in tissue culture and recovered from the fluid medium of the tissue culture. Then the protein jacket of the virus was removed and the viral nucleic acid isolated and injected into embryonic cells in tissue culture. When the medium from this tissue culture was injected into hamsters, it caused tumors in 100 percent of the animals within 18 days. When the enzyme DNase was added to the isolated nucleic acid it became noninfective, but was resistant to the action of RNase. Results of direct inoculation of nucleic acid preparations into animals will be reported later.

The results of these studies suggest that the nucleic acid of the SE polyoma virus is DNA, and that the latter is infective when extracted and purified from a virus suspension.

Juice of the abalone found to possess antimicrobial effect

The search for antiviral and antibacterial agents has been largely concentrated in the field of microbial products. However, the abundance and variety of organic materials in sea water, and the known ability of certain mollusks to filter and concentrate supended solids of their aquatic milieu, led Dr. C. P. Li, Laboratory of Virology and Rickettsiology, to study the abalone as a potential source of antimicrobial agents .

As reported in the Proceedings of the Society for Experimental Biology and Medicine, Dr. Li has demonstrated the antimicrobial action of fresh abalone juice against *Staphylococcus aureus*, as well as a protective effect of canned abalone juice against experimental poliomyelitis in mice.

At the beginning of his study, Dr. Li tested the inhibiting effect of canned abalone juice on *S. aureus*, but found the results to be inconsistent. Fresh abalone juice, however, demonstrated a consistent and marked antimicrobial activity against *S. aureus*. Furthermore, when the juice was heated to 95° C. for 45 minutes, or dialyzed against water overnight, no impairment of its effect was evidenced.

In testing the effects of abalone juice in experimental poliomyelitis, Dr. Li inoculated groups of Swiss mice with each of the three types of poliovirus, and fed the gastropod product to the treated mice in their regular diet. The rates of paralysis and death were 20 to 50 percent lower in the treated animals than in the controls. Moreover, the incubation periods were, in general, several days longer in the treated mice.

The thermostability and nondialyzability of this agent suggests that it is not an ordinary antibiotic. One of the chief advantages of its possible use for therapeutic purposes is that it is edible as a food. Further work on purification and concentration of the agent is in progress.

Virus growth of cell cultures maintained with skim milk medium

A study to determine the sensitivity of various tissue cells in culture maintained with skim milk medium indicates that the medium is free of inhibitor for infectivity and permits full sensitivity to infection by viruses tested.

The development by Dr. Samuel Baron, Laboratory of Viral Immunology (Science. 1958), of a serum-free medium containing skim milk which effectively maintains a wide variety of cell cultures, led to the present study of viral sentitivity of various cell cultures in this medium.

Comparative titrations by Dr. Baron and coworkers of 22 different virus strains showed that the infectivity titers of Echo, Coxsackie, poliomyelitis, influenza, herpes, measles, and vaccinia viruses in the presence of skim milk medium were equal to or greater than those obtained when established maintenance medium was used.

Strains of adenovirus maintained in skim milk showed a lower infectivity for the cells than in established maintenance media. Experiments to determine whether the skim milk acts directly to repress adenovirus multiplication or whether it lacks the cell-mediated enhancing factor of other media indicate that its inhibitory action was probably an effect on the tissue culture cells rather than an antiviral effect. Similar cell-mediated effects have been observed by other investigators.

The overall results of this study confirm the suitability of skim milk as a maintenance medium. Full details of the study by Alice Gochenour and Dr. Samuel Baron, laboratory of viral immunology, were reported in the "Proceedings of the Society of Experimental Biology and Medicine."

Selective inactivation of animal viruses in suspensions of live polio virus

Dr. Caspar Hiatt and coworkers, laboratory of biophysics and biochemistry, discovered that when minute quantities of toluidine blue dye (1 to 10 parts per million) were added to monkey kidney tissue culture fluids containing both polio virus and B-virus, the latter became the target of subsequent bombardment with light energy and was destroyed, while polio virus showed no significant loss of infectivity.

In 1958, Dr. Hiatt, in studying the effect of light on viruses in the presence of toluidine blue, had found that while many animal viruses become sensitized for photodynamic inactivation on subsequent exposure to visible light, others—including polio virus—are highly resistant to this treatment.

B-virus is one of the 40-odd wild viruses that have been encountered in the routine testing of the killed poliomyelitis vaccine. Since these contaminating agents are even more readily inactivated by formaldehyde than are the polio virus, they introduce no hazard in the killed vaccine. However, elaborate precautions and tests have had to be devised to make certain that they are not present in live polio virus vaccine since no way has been found to inactivate them without also inactivating the polio virus.

Little is known of the pathogenicity for many of these animal viruses, except for the B-virus which, although it causes only a mild illness in monkeys, is capable of producing fatal encephalitis in human beings. Sixteen such infections, 14 of them fatal, have occurred since 1937 in laboratories in England, Canada, and the United States among personnel engaged in research with monkeys and monkey tissue material.

Since a number of animal viruses can now be inactivated by this selective method, it may be of practical use as an added safeguard in the manufacture of live polio virus vaccine.

Formation of true antibody by hypogammaglobulinemic patients indicated

Despite the characteristic limitation of gamma globulin formation, persons with hypogammaglobulinemia are usually resistant to a second attack of a viral infection. Since antibody formation in these patients is usually undetectable by standard tests, resistance generally has been attributed to a nonantibody immune mechanism.

In a collaborative study, DBS and NIAID scientists have detected what appears to be naturally acquired neutralizing antibody to polio, ECHO, and Coxsackie viruses in the serum of persons with hypogammaglobulinemia (reported in the New England Journal of Medicine).

Using a highly sensitive technique (immunoinactivation plaque-neutralization tests), the serums of two patients with congenital hypogammaglobulinemia and of five with acquired hypogammaglobulinemia were found to have neutralizing capacity for a number of enteroviruses. The plaque-neutralizing material in the serums of these patients has properties of true antibody: (1) it is heat stable, and (2) the reaction of the antibody with the virus is time-dependent—two factors which do not obtain with nonspecific inhibitors.

In a subsequent study, Dr. Baron and coworkers, Laboratory of Viral Immunology, tested the antibody response of four hypogammaglobulinemic patients to a 10-ml inoculation of poliomyelitis vaccine, followed by a 1-ml dose 1 month later. Three of the patients, prior to inoculation, had low antibody titers to all three types of polio virus. Following inoculation, no significant rise in antibody occurred in two but the third had a small but definite increase to types 2 and 3 after the second inoculation. The fourth patient had preexisting antibody to types 2 and 3 polio virus, but none to type 1. Following the first inoculation, extremely small amounts of type 1 antibody, which diminished during the third week and increased significantly following the second inoculation, were detectable in this patient. No change in concentration of type 3 antibody was observed.

The result of this second study indicates that hypogammaglobulinemic patients may have a primary or secondary antibody response following exposure to an antigen, but the maximum obtainable antibody levels are severely limited. One possible interpretation of these findings is that the low levels of antibody in these patients are sufficient to confer immunity to viral diseases but insufficient to confer immunity to many bacterial and fungal diseases.

Deterioration of stored albumin detected by sensitive method

The problem of stability of normal human serum albumin during storage is of practical as well as theoretical interest. For example, when held in a stockpile, it must be able to withstand storage and shipment under various temperatures without significant change.

A long-term project has been undertaken in the Laboratory of Blood and Blood Products to determine what changes occur in stored albumin, the conditions affecting these changes, and the most suitable methods for detecting protein alteration. One phase of this study, reported by Dr. J. S. Finlayson and coworkers, in the Journal of Clinical Investigation, shows that the coordinated use of chromatography and ultracentrifugation provides a sensitive method for detecting alteration in normal human serum albumin during long-term storage.

The study was carried out on commercial human albumin preparations which had been stored for at least 5 years under various conditions. Indications were that the extent of changes occurring in albumin during storage are dependent on both the nature of the material used for preparation and the conditions of storage.

There was minimal difference between the chromatographic behavior of the albumin samples prepared from citrated whole plasma and stored for 5 years at 5° C. and the chromatographic behavior of fresh albumin samples either prepared commercially or in DBS laboratories. However, albumin stored for 10 years at 5° C. or for 5 years at 32° C. (with or without prior storage) demonstrated marked differences in chromatographic properties, as did albumin prepared from ultraviolet-irradiated dried plasma.

Fractions of albumin separated by chromatography were subjected to ultracentrifugation. The concomitant use of both techniques permitted measurement of protein components not readily observed by using either technique alone.

The clinical significance of any of the differences noted is not presently known: however, the alterations in physical-chemical character of albumin under certain conditions obviously warrant further investigation of the problem.

Studies initiated by Dr. J. T. Tripp, Chief of the Laboratory of Blood and Blood Products, using other techniques such as electrophoresis and viscosity are being continued. The work of Dr. Finlayson and coworkers indicates, however, that the chromatography-ultracentrifugation technique offers a sensitive method for the detection of protein changes in stored serum albumin.

Progress in development of measles vaccine

In order to assess and correlate the progress made in the development of a measles vaccine since their last meeting in 1958, investigators from university and pharmaceutical laboratories were invited to present their findings at a daylong conference at the Division of Biologics Standards on November 18. The meeting, chaired by Dr. Roderick Murray, Director, DBS, was attended by more than 50 virologists.

Dr. John Enders, whose work with measles virus established the principles for an attenuated measles vaccine, summarized his recent experience with the Edmonston strain of virus grown in chick embryo cells. Clinical data presented by other groups using live vaccine made from this strain gave evidence of its capacity to elicit satisfactory protection against natural measles as well as specific antibodies among the vaccines.

The Enders vaccine was shown by three groups of investigators to give 100 percent protection in children exposed to natural virulent measles virus, while the unvaccinated controls showed the expected high incidence of the disease. Evidence of satisfactory antibody titer at the end of 18 months was also presented. To date, close to 1,000 children have been given this vaccine.

The Enders vaccine, in most cases, caused some clinical reaction—principally fever. However, when administered concurrently with gamma globulin, such reaction was virtually nonexistent. This so-called active-passive immunization was favored by two groups of investigators but additional studies are necessary.

Although various methods of preparing the vaccine have been used, propagation in chick embryo tissue culture is preferred, since adventitious agents which might be pathogenic for man are less likely to be encountered.

There has been some question in the past whether a live vaccine of sufficiently high titer could be produced which would maintain its potency during storage. It is now generally agreed that it is possible to stabilize the vaccine in the dry state.

Studies with both experimental animals and human subjects have given assurance that the Enders strain is devoid of deleterious neurotropic effect. Dr. Frederic A. Gibbs, University of Illinois School of Medicine, and his colleagues, using electroencephalography for determining neurologic reaction showed that approximately 50 percent of children develop significant abnormalities in their EEG patterns during the course of natural measures. In contrast, no such changes were evident in children inoculated with the Enders attenuated vaccine. This would indicate that central nervous system involvement, which does occur in natural measles, rarely if ever occurs with attenuated vaccine.

Dr. Harry Meyer, Laboratory of Virology and Rickettsiology, DBS, outlined the work being done in DBS laboratories in developing serologic tests for detection of measles antibodies. Methods for preparation of a dried reference serum are also being investigated for use in both the complement fixation and neutralization tests. The standardization of gamma globulin preparations for measles antibody content is also planned.

Work will be continued by the various investigative groups in acquiring a larger clinical experience. DBS will continue to coordinate these studies and to encourage the acquisition of new data.

DBS research study presented at SEATO–NIH Cholera Conference

A mouse protection test for the assay of cholera vaccine, developed by Dr. John C. Feeley and Dr. Margaret Pittman, Laboratory of Bacterial Products, was presented at the first of the conferences on cholera, sponsored by the Southeast Asia Treaty Organization. The 4-day conference was held in December in Dacca at the recently established laboratory for cholera research in East Pakistan, where the disease is endemic.

International reference cholera vaccines of the Inaba and Ogawa types of *Cholera comma* were established in 1948 by the World Health Organization but without a unit of potency, because of failure of collaborative assays. Two years ago, WHO's interest was renewed and a Study Group in which Dr. Pittman participated formulated recommended requirements for cholera vaccine. The need for comparing laboratory potency values with prophylactic efficacy in man was emphasized and the development of a mouse protective test to evaluate the potency of cholera vaccine quantitatively was initiated by DBS in anticipation of clinical trials to be carried out by the WHO.

The major emphasis in Dr. Feeley's work has been the standardization of the variables which influence the test, as well as the selection and preservation of a U.S. reference vaccine to determine its relative potency. Difficulty has been encountered in preserving the potency of the reference vaccine during freeze-drying and various methods are now under investigation.

Using the mouse protection test, reproducible relative potencies of vaccines prepared in other countries, as well as the WHO reference preparations, have been determined. It has also been possible to determine the mouse cross-protection of the two *C. comma* types, Ogawa and Inaba—a problem which has received much attention in the past.

Although the DBS test is feasible for the evaluation of the mouse protective potency of cholera vaccine, clinical trials of vaccine of known laboratory potency must be carried out before its relation to epidemiologic effectiveness can be evaluated.

PROGRAM DEVELOPMENTS

DBS building dedicated June 30

The formal dedication of the Division of Biologics Standards Building took place on June 30. His Majesty Bhumibol Adulyadej, King of Thailand, officially dedicated the building by unveiling an inscribed bronze plaque, which will be placed in the main entrance of the building.

Their Majesties, King Bhumibol and Queen Sirikit, who arrived for a 4-day state visit in Washington on June 28, were guests at a luncheon given by Secretary and Mrs. Flemming at Stone House preceding the dedication ceremonies.

The invitation to participate in the dedication of the new DBS laboratories was extended to King Bhumibol because of his active role in health measures in his own country and his interest in the South East Asia Treaty Organization-National Institutes of Health cholera research project.

During the 1958–59 chlorea epidemic in Thailand, the work of United States and Thai scientists demonstrated, through greatly reduced death rate, the value of collaborative research. The U.S. Cholera Research Advisory Group which visited the SEATO and other Asian countries last year was granted an audience by King Bhumibol in Bangkok. The group was headed by Dr. Joseph E. Smadel, former NIH Associate Director for Intramural Research, who assumed his new duties as Chief of the DBS Laboratory of Virology and Rickettsiology in July.

Sterility test procedures for biological products revised

The revision of one of the basic tests designed to insure the purity of all licensed biological products reflects recent advances in manufacturing procedures as well as in scientific achievement.

The revised procedures for sterility testing, which manufacturers of biological products subject to control under the Public Health Service Act are required to follow, became effective on April 15. Redesignated as section 73.73 of the Public Health Service Regulations, these requirements are designed to insure the freedom from extraneous micro-organisms of all licensed biological products. The revision represents a composite scientific opinion based on years of research.

The timeliness of the adoption of U.S. sterility test standards is emphasized by the recent recommendations of the World Health Organization. The participation of Dr. Margaret Pittman, Chief, Laboratory of Bacterial Products, DBS, in the WHO study group which formulated these recommendations at the Geneva conference in 1958, facilitated the efforts of DBS in drafting comparable requirements. Although the U.S. standards are more detailed and specific, they are consistent with those recommended by WHO. This should be of considerable help to those U.S. producers of biologics engaged in foreign commerce, as well as to foreign manufacturers who export biologics to this country, since the latter must also be licensed to comply with U.S. standards.

British laboratories study DBS live polio virus research

Indicating the worldwide interest in the control problems peculiar to the live polio virus vaccines, three British virologists visited DBS laboratories early in January. Representing their respective laboratories in the field of live polio virus vaccine research, were Dr. Alan P. Goffe, of the Burroughs-Wellcome Laboratories, Kent; Dr. J. A. Dudgeon, of the Virus Research Unit, Glaxo Laboratories, London; and Dr. Thomas Beswick, of the Medical Research Council Laboratories, London.

Of general interest were slides showing the histologic lesions of the brains and spinal cords of monkeys inoculated with live attenuated polio virus. The slides corroborated the data reported by DBS scientists at the World Health Organization-Pan American Health Organization live polio virus conference last June. The report, "Comparative Virulence for Rhesus Monkeys of Polio Virus

Strains Used for Oral Administration," by Dr. Murray, et al, was published in the "Proceedings of the First International Conference on Live Polio Virus Vaccines."

Soviet-American Polio Conference Mutually Profitable

The first mission to take place under the United States-U.S.S.R. exchange agreement of November 1959 was the Soviet-American meeting on poliomyelitis control held in Moscow early in May. Attended by 13 American and 15 Russian scientists, the meeting was devoted chiefly to technical discussions of research, production, and testing of live polio virus vaccines.

The Russians reported the successful use of the oral vaccine developed by Dr. Albert Sabin, director of research at the Children's Hospital, Cincinnati. The Russian-produced Sabin vaccine had been given to 60 million Russians 2 months to 20 years of age. Russian scientists voiced the hope that this method of control will completely eradicate the disease in Russia within the next year or two. They agreed, however, that further studies of effectiveness and duration of effectiveness were needed.

The American scientists described U.S. experience with the killed poliomyelitis vaccine, which had been given to more than 90 million persons in this country, and the field trials with the live polio virus vaccines of Drs. Sabin. Koprowski, and Cox.

The discussions indicated that, while the proposed production and testing standards of both countries are parallel in most respects, certain differences exist. It was agreed that further exchange of information and comparative studies is desirable and that such information be provided to the World Health Organization with a view to the ultimate development of international recommendations.

Americans attending the meeting were Dr. David Price, Chief of the U.S. delegation and personal representative of the Surgeon General; Dr. Sabin; Dr. Koprowski; Dr. Benyesh-Melnick, and Dr. Joseph E. Melnick, Baylor University School of Medicine; Dr. Theodore E. Boyd, National Foundation; Dr. Victor Cabasso, Lederle Laboratories; Dr. Eugene Flipse, University of Miami School of Medicine: Dr. John P. Fox, Institute for Public Health Research, New York City; Dr. Thomas Francis, University of Michigan; Dr. Herman Kleinman, Minnesota Health Department; Dr. Alexander Langmuir, CDC; and Dr. Roderick Murray, Director DBS.

The Russian delegation was headed by Dr. V. M. Zhdanov, Secretary of the Academy of Medical Sciences of the U.S.S.R., and included Dr. M. P. Chumakov, Director of the Institute for Poliomyelities Research in Moscow, and other virologists, epidemiologists, and research scientists.

Recommendations for live polio virus vaccine production

After extensive study of all three candidate strains (Sabin, Cox, and Koprowski) the PHS Committee on Live Polio Virus Vaccines met August 19 with technical representatives of interested drug firms and with DBS staff to review the proposed requirements for the manufacture and testing of live polio virus vaccine.

The committee recommended the Sabin Type I and II strains as possessing the most favorable laboratory and field characteristics. The Sabin Type III was recommended as being satisfactory from the standpoint of neurovirulence, although it has less than optimal immunogenic capacity and shows a tendency to change its neurovirulence characteristics after passage in man. Neurovirulence for monkeys is considered the most important laboratory criterion available, and the intrathalamic test in monkeys has been recommended for adoption as a test for neurovirulence.

The committee also recommended that when it becomes available, live polio virus vaccine be used on a community rather than on an individual basis. This recommendation was made principally because of the potentiality of reversion to virulence of the live virus strains. In the field studies, the vaccine has been largely employed in mass administrations with the vaccine given simultaneously to the population thus permitting little opportunity for serial human transmission of the virus; or the vaccine has been administered during a time of the year when "wild" virus strains have usually shown limited capacity for spread.

The Surgeon General announced his acceptance of the committee's recommendations in a press conference on August 24. Problems raised by the committee regarding the optimal use of the vaccine are to be taken up with appropriate advisory groups, such as the State and Territorial Health Officers and representatives of the medical and health professions and of the voluntary health agencies.

The recommendations, which were made available to those manufacturers interested in the eventual production of the vaccine, will serve as the basis for the eventual adoption of regulations for live polio virus vaccine. Manufacturers who make application, demonstrating the necessary experience and ability to produce a vaccine which conforms with the regulations, will be licensed.

It is not anticipated that the live polio virus vaccine will be available in substantial supply before mid-1961.

Live polio virus vaccine recommendations well received abroad

Recommendations of PHS Committee on Live Polio Virus Vaccine were presented by Dr. Roderick Murray, Director, DBS, at the Sixth International Congress of Microbiological Standardization in Weisbaden in September. Members of the Congress appeared well satisfied with the progress made in the United States in the development of standards for live polio virus vaccine. Dr. Murray discussed the recent recommendations of the PHS Committee on Live Polio Virus Vaccine as they affect the production of the vaccine. Copies of the recommendations were distributed to Members of the Congress.

Dr. Albert B. Sabin, of the University of Cincinnati, also spoke on the subject of live polio virus vaccine. Dr. Sabin summarized his work and described the technique he uses for intraspinal inoculation of monkeys.

Scientists from more than 20 nations attended the Congress, which serves as a means for exchanges of scientific information. Although essentially composed of European biological manufacturers and interested representatives of control agencies and microbiological laboratories, the presentations at the annual meeting cover a rather broad area of the biological field, including human and veterinary biological products as well as such problems as the testing of disinfectants.

The two Russian scientists invited to present papers were unable to attend the conference.

Exchange of scientific information enhances DBS research program

The exchange of ideas and technical knowledge with other laboratories working in related areas has proved to be of inestimable value to the DBS research programs.

Dr. Gerald L. Van Hoosier, Laboratory of Virology and Immunology, returned to DBS in August after a year's study under Dr. Edwin H. Lennette, chief of the Viral and Rickettsial Disease Laboratory.

HIGHLIGHTS OF PROGRESS OF RESEARCH IN GENERAL MEDICAL AND AND BIOLOGICAL SCIENCES, 1960

ITEMS OF INTEREST ON RESEARCH STUDIES SUPPORTED BY THE DIVISION OF GENERAL MEDICAL SCIENCES

The Division of General Medical Sciences was established at the National Institutes of Health in 1958 as an agency for the administration of grants programs. A prime objective of these programs is to strengthen research which will foster systematic knowledge of the natural phenomena which underlie organic disease generally. With this, the strengthening of clinical research and academic and technological resources oriented more directly to the conquest of disease is an increasingly important function of the Division's grants programs.

Unlike the Institutes of NIH which are oriented to specific diseases, the responsibility of the DGMS encompasses inquiry into the structures, processes and relationships which comprise the entire organism and constitute the organic and physical substrate of all our major disease problems. Appropriate inquiry into any aspect of the natural order which shows promise of yielding new knowledge of the organic factors which underlie disease may warrant DGMS support. This may include the design of analytical instruments, tools, and methods, and the development of new perceptual constructs and systems of inductive reasoning which show promise of engendering such knowledge by their proposed application.

In addition, the Division administers NIH grants programs for training investigators in the disciplines basic to medical research, and it directs the NIH Center for Aging Research. The Division also has responsibility for certain disease-oriented programs—research of an applied nature which is not encompassed by the disease-oriented institutes of NIH.

Following are a few examples of research findings, selected for their interest value and as illustrative of major areas of program activity in the Division during 1960. Some of these findings have implications for clinical medicine which are already apparent; others have implications for the solution of practical problems in environmental health. Most are basic—welcomed within the technical disciplines primarily for their ability to close gaps in the body of general knowledge which serves as the foundational structure of clinical medicine. The practical usefulness of most of the latter findings can only be assessed after they have been assimilated from the technical literature by investigators and practioners in medical fields and incorporated into new approaches to research and clinical problems.

BASIC BIOMEDICAL FINDINGS

Clearer definition of the gene from Texas studies in bread mold

NIH grantees at the University of Texas are exploiting the genetic and nutritional simplicity of the red bread mold *Neurospora* to map the locations, on particular chromosomes, of the determinants of biochemical reactions by which particular substrates are metabolized for utilization in life processes. The work is expected to lead to a clearer definition of the gene.

The red bread mold *Neurospora* has long been regarded as one of the most useful of genetic experimental organisms. Pure strains can be multiplied a millionfold in a few days without genetic change. Each cell nucleus contains only a single set of genes, so recessive characters are not hidden by dominants, as they are in organisms with the double set, such as man. *Neurospora* can be grown in pure culture on a chemically known medium containing only sugar and a B vitamin (Biotin) plus a few inorganic substances. In the natural state, the mold possesses the biochemical apparatus to make, from these simple materials, all the other constituents of its cells. Thus when a genetic element is experimentally disrupted by irradiation the mutation may be expressed and mapped in terms of the measurable changes which occur in the simple nutritional requirements of the organism.

A large group of such nutritional mutations of *Neurospora* is described in "Proceedings of the National Academy of Sciences" by R. P. Wagner, C. E. Somers, and A. Bergquist, at the University of Texas in Austin. Plotting the distribution of the mutations on a map of *Neurospora's* chromosomes, Wagner's group traced all of them to a limited area of the fifth chromosome. Wagner's report appears to record the first demonstration, in any organism with single or double chromosome complement, of a direct relationship between one small segment of a single chromosome and a particular set of biochemical reactions. (Damage in the segment of chromosome directly affected the transformation of precursors of two important amino acids—isoleucine and valine.)

The results also strongly indicate that there is a linear arrangement of the chromosomal material, with the active elements of it arranged to correspond to the order of sequence of the biochemical reactions it controls.

Further understanding, valuable in genetics, of what genes are and how they work is expected to result from continued study of the *Neurospora* system.

Wagner's work is supported by the Division of General Medical Sciences and the National Cancer Institute.

Bread mold cells serve as living centrifuge tubes for cytochemical studies

The tough cylindrical cells of *Neurospora* (red bread mold) tendrils have been found to serve as living ultramicrocentrifuge tubes, allowing the constituent organelles and fluids of the cell to be grouped in layers for biochemical analyses without the necessity for disrupting vital interrelationships. (Cells subjected to 50,000 gravities recover, their organelles regroup, and they continue to grow.) This is reported in "Experimental Cell Research" by Marko Zalokar of Yale.

Zalokar reports that the order of sedimentation, or layering of cell constituents by centrifugal force, in the living cell is almost the direct reverse of that which results when the cells are first homogenized—a conventional cytochemical technique. The pattern of centrifugal distribution of genetically important substances, such as DNA, in relation to the cell organelles, is also different when living, instead of homogenized, cells are used.

Zalokar points out that much of the progress of modern biochemistry has depended upon the development of methods which do not break down major cell components, even though the cell itself has had to be sacrificed. The availability of a method for biochemical studies during life of the constituents common to all living cells should further genetic and immunologic knowledge of the mechanisms of molecular duplication such as protein synthesis, which are thought to be fundamental in cell reproduction and the determination and maintenance of the biological individuality (characteristic structural and functional detail) of each life form.

Gene for mouse dwarfism acts first on pituitary, not on the hypothalamus

The question has been raised whether the gene that produces dwarfism in anterior pituitary dwarf mice acts on the pituitary directly, or indirectly through the hypothalamus. Experiments in pituitary transplantation provide convincing evidence that the pituitary gland, not the hypothalamus, is the primary site of action of the dwarfism gene.

Since 1929, when the strain was discovered, the pituitary dwarf mouse has been studied extensively for insights into the nature of human endocrine disorders, including human genetic pituitary dwarfism. As in some of the human conditions, the hereditary dwarfism of the mouse is known to involve arrested development of the anterior pituitary structures which secrete growth hormone, and transplants or injections of normal pituitary material are known to promote normal growth in the dwarfs. Although it is obvious from this that the gene for dwarfism acts on the pituitary gland, the possibility exists that the pituitary effect is a secondary one—that some undefined lesion of the hypothalamus (through which nervous control of some pituitary secretions is mediated) underlies the pituitary deficiency.

An answer to the question of which of the two structures is the primary site of action of the gene has been provided by Robert L. Carsner and Edward G. Rennels of the University of Texas Medical Branch, Galveston.

They report in Science that surgical substitution of normal anterior pituitary glands for dwarf pituitaries (between immature littermates) resulted in mice which, though genetic dwarfs, had the appearance and growth rates of normal mice. But substitution of anterior pituitary from dwarf mice in genetically normal littermates resulted in dwarfed mice, despite their possession of the genetically normal hypothalamus. This shows rather clearly that the anterior lobe of the pituitary and not the hypothalamus is the primary site of gene action in the anterior pituitary dwarf mouse.

Theory of aging implies dependence of sex ratio at birth on father's age

Leo Szilard, noted nuclear physicist and theoretical biologist at the University of Chicago, developed a general theory of aging applicable to mammals, during his recent tenure as a consultant to the basic research program of NIMH. The theory assumes that whole chromosomes suffer complete loss of function in single random events ("aging hits") during the lifetime of the individual.

On the basis of this theory, Szilard has derived from American life tables the frequency with which such aging hits should occur in the somatic cells in man. The calculated frequency is once every 12 years, on the average.

Assuming this mechanism and frequency of chromosome loss holds for the immature germ cells which give rise to sperm (the spermatogonia), Szilard reasons that the ratio of boys to girls at birth should decrease with the age of the father.

He consulted the birth data for the United States for 1955 to compute the relationship of the ratio of boys and girls to the ages of their fathers. His calculations from this record of actual events indicate a fall did occur, with increasing paternal age, in the ratio of boys to girls at birth. However, he concludes, data based on larger population samples than the 1955 record must be available before it will be possible to draw conclusions relevant to his theory.

Szilard's work on the frequency of aging hits in man and the relationship to sex ratio is published in Nature.

Evidence for RNA role in synthesis of antibodies

Seeking the source of the immune response by which organisms "learn" to recognize and destroy foreign proteins, an Israeli team with DGMS support has gained evidence of antibody production and storage in the protein which occurs in combination with ribonucleic acid (RNA) in the cells of antibody-forming organs.

The nucleic acids DNA and RNA are best known as vehicles for the patterns of life's continuity in genetic reproduction—DNA in the genes as chemical repository of the individual protein codes which are the blueprints of the species, and RNA as the cytoplasmic "template" in which each of the protein constituents of cell, organ, and organism is reproduced in conformity with its particular DNA code.

The minute cytoplasmic particles in which the RNA of protein-producing cells is concentrated were reported earlier by NIAMD grantees in Boston to contain much protein which is bound with the RNA in a chemical complex. Thus the RNA actually occurs in those particles as ribonucleoprotein, and the particles themselves have been termed "ribonucleoprotein particles" by the Boston workers.

The 1960 DGMS-aided work, by a team at the Weizmann Institute in Rehovoth, Israel, supports the idea that the ribonucleoprotein complex of the cell may play a role in the synthesis of antibodies. This concept was suggested earlier by less definitive work done in Czechoslovakia.

Although the Weizmann findings do not permit conclusive definition of the role of ribonucleoprotein in antibody synthesis, the investigators observed that the antibody response in their experimental animals involved a marked increase in the ribonucleoprotein content of the antibody-forming organs and that the protein part of the ribonucleoprotein complex obtained from these organs contains inactive antibodies which are released in active form on destruction of the ribonucleic acid part of the complex.

The findings accord with the idea that the antibody molecule (which is itself a protein) forms part of the ribonucleoprotein complex of the cell and that this complex is the site of synthesis of antibody, according to the Weizmann investigators.

M. Feldman, D. Elson, and A. Globerson of the Weizmann team published the findings in Nature.

Antibody formation after antigen is gone occurs for many or all antigens

Continuous synthesis of antibody long after a single injection of the antigen, occurred in rabbits in response to bovine serum albumin, guinea pig serum protein, and egg albumin and its azo derivatives. The findings, by Maxwell Richter and Felix Haurowitz, of Indiana University, Bloomington, show for the first time that continuous antibody formation long after primary immunization, is stimulated not only by the carbohydrate antigens, toxoids, and viruses, but also by typical innocuous protein antigens.

This has important implications for understanding the secondary response (and associated sensitivity reactions). Failure to detect circulating antibody months after introduction of an antigen, followed by the rapid appearance of precipitating antibody upon a second exposure, is often attributed to "memory" of the antibody-producing cells for the departed antigen (hence the term "anamnestic" reaction for this phenomenon). According to the Bloomington work, the reintroduced antigen, even when given months after the primary immunization, is being given to an organism which is still making the antibody.

In every instance, the Bloomington investigators were able to detect the antibodies in the circulation for months after a single antigen injection—but not by using the conventional precipitation methods of antibody detection. The presence of the antibodies was demonstrated only by the agglutination of antigen-coated red blood cells. The antibodies were of the nonprecipitating type.

With the application of techniques which do not depend on the precipitability of the antibody it will undoubtedly be demonstrated that maintenance of antibody synthesis for a long period of time after antigen administration is a universal phenomenon and not an isolated observation which depends on the nature of the antigen used," Richter and Haurowtiz predict in the Journal of Immunology.

Female survival advantage extends to first weeks of embryonic life

Sex determination by chromosome count in the placenta is extending knowledge of the sex ratio in human mortality throughout the prenatal period. Evidence thus far indicates that the female advantage over the male in infant survival extends back to the earliest days of pregnancy.

Investigators of the State University of New York, New York City, have used sex chromatin to determine gender in 242 prenatal deaths at from 1 to 24 weeks of gestation. They found only 93 females and 149 males—a ratio of 100: 160.2.

The findings, though preliminary, indicate that it is the male who makes up the greater part of early pregnancy wastage, as he does the mortality of infants over 1,000 grams (the perinatal mortality).

Fresh placental tissue, obtained at the time of currettage for incomplete abortions, was used. Basing judgment of sex on the chromatin of placental, rather than fetal cells, the New York group was able to extend sex determination back to the first week of pregnancy, and make determinations even when the embryo itself was not available.

No correlation was found between sex ratio and gestational age of the miscarried fetuses.

The results may seem surprising by some present lines of reasoning. For example, according to present knowledge of the mechanism by which the paired chromosomes divide as the sex cells mature, there should be as many male as female-determining sperm (half the sperms are X-bearing and half Y-bearing). Thus, one may expect a sex ratio of 1 to 1 at the time of fertilization. Since the accepted sex ratio at birth the world over is about 106 males to 100 females, one might expect that more females than males die in the earliest months of pregnancy.

This has been one of the speculations—there was no way to determining the reality until Barr's recent discovery of the microscopically visible sex difference in the chromosomes, and the present accumulation of data. The data thus far suggest that the sex ratio in man at the time of fertilization may be about 111 to 100, male to female. More data is needed before the true primary sex ratio can be established with certainty.

Vincent Tricomi, David Serr, and George Solish published the findings in the American Journal of Obstetrics and Gynecology.

Normal development of public symphysis in abnormal location

Evidence that the public symphysis can develop normally when transplanted out of its normal site, and that the transplant retains its ability to respond specifically to estrogen and relaxin at maturity, is published by E. S. Crelin of Yale, in the Anatomical Record.

The findings indicate that the ability of the symphysis to respond to these hormones at the time of life when they are active (sexual maturity, pregnancy, and delivery) is innate in the tissues of this pelvic joint ("* * * predetermined by the immature tissue from which the symphysis develops").

Crelin reports that the public symphysis (including its cartilage and the angles of the public bones) was transplanted into the muscle of the chest (pectoralis muscle) in 50 immature (12 day) mice. Half of the mice received injections of estrogen and of a relaxin preparation at 4-day intervals for 18 days prior to the time the transplants were finally examined at 8 weeks of age.

With few exceptions, he reports, gross and histologic examinations of the transplants of the untreated mice showed they had developed into public symphyses essentially identical to those of normal virgin adults. The transplants of the hormone-treated mice had undergone the normal interpubic transformation specific for such pelvic tissues (resorption of bone in response to estrogen, and changes in the ligaments, related to their normal relaxation during pregnancy and delivery).

Advance in chromatography may aid research on roles of major biogenic amines

Jorge Awapara, Virginia Davis, and Odette Graham, of the Rice Institute, Houston, Tex., report the development of column chromatographic methods enabling complete separation of a number of naturally occurring amines from their parent amino acids and from some of their derivatives.

Thus a step has been taken toward elimination of one of the difficulties in detecting small amounts of amines in tissues—the fact that they are indistinguishable from their parent amino acids by many of the known tests. Using known mixtures of various amino acids and amines in comparing conventional testing methods with their own innovations, the Houston workers achieved the desired separation and quantitation by column chromatography in which the stationary phase was cellulose and the mobile phase a mixture of butanol-acetic acid-water. They tested the method in the identification of hordenine in germinating barley (where it accumulates in the roots in the first week of life), and found large amounts of hordenine and eight other amines as well.

The part played by amines in life processes has been attracting the interest of investigators in virtually every major field of biologic science. Many drugs are believed to exert effects by influencing amine metabolism. In most animals and bacteria, amines appear to be made from their parent amino acids by decarboxylation. In this connection, it may be of interest that the Rice Institute workers suggest that a relatively easy method for measuring amino acid decarboxylases may be developed as an extension of their reported work.

There work is reported in the Journal of Chromatography.

Oxygen-carrying capacity of respiratory pigments demonstrated experimentally

In vitro experiments by P. F. Scholander at Scripps Institution of Oceanography, La Jolla, Calif., have indicated that under steady-state conditions and at low tension, oxygen may be transported as much as eight times as fast by a solution of human hemoglobin as by water. Increasing the pressure 1 atmosphere has the effect of doubling the rate of transport. The same effect occurs in intact red cells and in myoglobin, the respiratory pigment of muscle.

The transfer of oxygen to the cells of the body is essential for the maintenance of life. The complexities surrounding the manner in which this transport is carried out have not been fully understood, however. It is clear that passive diffusion is a relatively slow process and that oxygen has a low solubility in water. The oxygen-carrying property of hemoglobin is the vital process which makes adequate tissue oxygenation possible. Among the pigments with oxygen-binding capacity, the hemoglobin of the red cell and the myoglobin of the muscle are most abundant in the body. Hemoglobin is transported rapidly to every part of the body, while myoglobin is confined within the muscle system and is stationary.

In his paper published in Science, Scholander has proposed that the system for transport of molecules resembles a conveyor belt or bucket brigade in which oxygen molecules are handed down from one to the next, in a chain. The idea is postulated for both hemoglobin and myoglobin.

Fetal hemoglobin may be an adaptation to deficiencies in the fetal environment

It is not known what causes the gradual decrease of the fetal form of hemoglobin in normally maturing infants, or the persistence of fetal hemoglobin in adults with certain inborn anemias, such as thalassemia. Some light may be thrown on the underlying mechanisms as a result of studies in Boston, Mass., showing influences of cellular environment on the relative quantities of fetal and adult hemoglobin synthesized by human immature red cells (reticulocytes).

David W. Allen and James H. Jandl used isotopic labeling techniques in in vitro measurements of fetal and adult hemoglobin formed in reticulocyte-rich suspensions of umbilical-cord blood drawn at the time of delivery. They found that deficiencies of oxygen and glucose favored the production of the fetal hemoglobin compared with the adult type in the suspensions.

This raises the possibility that the fetal hemoglobin is an adaptation to the environment of the fetus, wherein oxygen and glucose are at a premium, Allen and Jandl conclude. The possibility provides impetus for inquiry into defects of energy metabolism in congenital anemias of adults which are characterized by the persistence of large amounts of fetal hemoglobin, they suggested.

These findings are reported in the Journal of Clinical Investigation. Following submission of this report, similar observations agreeing with those of Allen's group were published by another research group (E. D. Thomas et al.) in the British journal Nature.

The Boston work is reported from the Thorndike Memorial Laboratory, Boston City Hospital, and Harvard Medical School.

Red-cell generating agent of "altitude goat" milk found active in rats

An erythropoietic (red-blood-cell generating) factor seems to occur in the milk of lactating goats exposed 4 hours daily to an altitude of 22,000 feet (simulated by decompression chamber). Evidence tentatively suggesting existence of the "erythropoietin" was published in the Physiologist in 1958 by J. Clifford Stickney and coworkers at West Virginia University in Morgantown. The West Virginia group reported then that four kids, maintained from birth on the milk of such "altitude goats," showed slightly higher hemoglobin levels and immature red-cell counts than did four control kids fed milk from goats kept at ground level. The West Virginia group reports in 1960 (federation proceedings) that extracts of the milk whey of three such "altitude goats" raised hemoglobin levels and reticulocyte (immature red cell) counts when injected into the peritoneal cavity in rats. These blood changes did not occur in control rats injected with whey material obtained by the same extraction method from the same three goats when they had not been subjected to the decompression and hypoxia of the "altitude" treatment. Thus, the activity of the erythropoietin in the "altitude goat" milk does not appear to be limited to the goat.

The role (or roles) of the erythropoietins in influencing red cell production in normal and disease states is poorly understood. Additional knowledge of erythropoietin origins and activities is valued for the light it may throw on mechanisms of hemoglobin and red cell production. This understanding could help solve practical problems of red cell and hemoglobin inadequacy in situations of tissue oxygen deprivation due to disease (as in anemias) and of atmospheric oxygen rarity (as in high altitude flying).

The 1960 work was published by Stickney, Theadore L. Browne and Edward J. Val Liere.

New centrifuge for study of gravity in control of mammalian growth

A multifield centrifuge capable of holding cages large enough for small mammals to be maintained under continuous high gravity for years is announced from the State University of Iowa, Iowa City. No such a centrifuge had been previously available commercially, and little experimental data have been available on the role of gravity as an environmental factor in the control of mammalian growth.

The centrifuge has been in continuous operation for over 18 months. Mice have been reared in it under high gravity conditions; and it is now being prepared for use with kittens.

The apparatus is described and illustrated by Gerald Walters, Charles C. Wunder and Lincoln Smith in the Journal of Applied Physiology.

Thigh bones show striking growth changes at four times earth gravity

Thigh bones of mice reared at four times the earth's gravity grow faster than other body tissues and assume a more circular cross-section, according to a study at the State University of Iowa, Iowa City. Although the explanation of this is not definitely known, the circular cross-section would give this supporting structure more strength with which to resist gravity.

The shape and size of body parts are believed to be influenced by gravity, although little data have been available on the role of this environmental factor in growth processes.

Having reared mice at four centrifugal gravities, the Iowa investigators report that the thigh bone effects of the gravity in female mice were more striking than any other effects. At first the experimental animals fell behind the controls in body mass, then continued to grow. But the femurs grew continuously from the start as fast as or faster than those of the controls, acquiring a more circular cross section.

Further work is necessary before actual causes of the bone changes are known, but the circular form would give the supporting structure more strength against gravity. Wolff's law proposes that mechanical force will evoke growth of the stressed part of the bone, and the artificial multiplication of earth's gravity in the experiments would certainly cause such stresses.

The observed general loss of body mass is attributed by the Iowa City workers to lowered food consumption during the first week in the centrifuge.

The data are published in Nature by Charles C. Wunder, Stanley R. Briney, Melvin Kral, and Charles Skaugstad.

Acoustic and respiratory significance of geometric configuration of larynx

B. Raymond Fink of the Presbyterian Hospital and Columbia University, New York City, and F. Kirschner of the General Electric Co., Bloomfield, N.J., in studies of the geometrical configuration of the larynx with X-rays, have observed that the cavity below the vocal apparatus forms an aerodynamic nozzle whose mouth looks into the trachea while the throat accelerates the flow toward the oral cavity. Respiratory air flowing through the larynx traverses a manifold section of two horns formed by the vocal folds and the vestibular folds. The system allows optimum flow during breathing. The research is reported in the International Journal of Phoniatry.

The investigators studied 11 women and 12 men, 4 of whom had unilateral laryngeal nerve paralysis and 1 bilateral paralysis. The use of X-rays, which were taken during slow expiration and phonation, made it possible to employ the living larynx as a model and to observe its configuration directly, without interference from instruments.

It was found that contraction of the vocal muscle within the vocal folds during expiration, inspiration, and speech, maintains the contour of an exponential nozzle between the vocal folds. The surface of the folds is convex, with an approximately exponential curvature, which has been shown to produce the lowest coefficient of resistance to airflow. In paralysis the vocal folds are prolapsed and their surface is concave. The values for the coefficient of normal flow resistance were computed from the hydrodynamic equation of flow and verified by direct measurements on models of five different types of acoustical connectors. The lowest resistance was obtained from the model fashioned after the human exponential connector.

The investigators found that there was acoustical significance in their study in that the exponential horn in the larynx serves as an acoustic transformer between the infralaryngeal and supralaryngeal cavities. It was of interest that the subject with the best trained voice in the studies also had the smoothest horn in the larynx.

The findings demonstrate that increased respiratory effort is required in cases of laryngeal paralysis, on the basis of the inefficient contour produced as well as the decrease in the diameter of the orifices.

Placental focus of uterine muscle control shown by substituting wax for fetus

Despite the experimental work of past decades establishing the role of progesterone in the maintenance of mammalian pregnancy, repeated failure of progesterone therapy to prevent abortive uterine contractions led many obstetricians in recent years to doubt the significance of this ovarian hormone in the maintenance of human pregnancy.

The inconsistent uterine effects of systemic progesterone were partly explained by the recent experimental studies of Arpad Csapo and others, indicating that the myometrial effect of progesterone is a local one that declines with increasing distance from the placenta. Csapo postulated that the level of progesterone in the general circulation is not of significance in the birth process, but that the local uterine concentration of the hormone—its diffusion from the placenta—is of major importance.

A research team at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, illustrated this placental localization of uterine muscle activity in rabbits by insertions of straight paraffin rods into the uterine lumen following removal of the fetuses (but not their placentas). Within 48 hours, marked curvatures and constrictions appeared in the rods. The constrictions occurred at points midway between adjacent placentas. The degree of rod curvature was related to the distance of the rod from the placenta.

"Since progesterone acts to dampen uterine contractions," the Bar Harbor group reports in "Fertility and Sterility," "it is clear that the muscle closest to the placenta is under a greater degree of progesterone control than the muscle furthest from the placenta. In this respect, these results are in harmony with the work of Csapo on the concept of a local gradient in the progesterone level in the uterine musculature."

The Bar Harbor studies were supported by DGMS and NIMH research grants. M. X. Zarrow, E. D. Wilson, A. Lee Caldwell, Jr., J. Yochim, and P. B. Sawin participated in the work.

FINDINGS PERTINENT TO ENVIRONMENTAL HEALTH

Cyanide problem in water pollution may yield to biological treatment

Using bacterial cultures (activated sludge system) like the ones used for sewage treatment, studies in Lancaster, Pa., have shown that inorganic cyanide can be inactivated by biological treatment without the further addition of sewage, the organisms coming to rely exclusively on the cyanide for their carbon and nitrogen nutritional requirements.

The inorganic cyanide wastes produced in metal plating and hardening processes are said to be among the most toxic wastes produced in industry. Not only are small quantities toxic to fish, but even smaller quantities may interrupt the natural purification processes of streams by killing off the responsible organisms. The same thing generally happens when cyanide gets into the biological treatment systems of sewage disposal plants.

Most present-day cyanide disposal methods are chemical processes expensive in their requirements for heat, electric current, chemicals, and the further disposal of such byproducts as toxic hydrogen cyanide gas.

Reporting in the "Journal of the Sanitary Engineering Division, Proceedings of the American Society of Civil Engineers," the Pennsylvania group credits the British Water Pollution Research Laboratory for most of the research done to date on the biologic inactivation of inorganic cyanide. The British workers had subjected complex metal cyanides to a continuing feed of sewage in trickling filters, with a view to subjecting the cyanide to the same complex of natural biologic and chemical activities which work so usefully on sewage. This was effective in demonstrating what the Lancaster group refer to as "the extreme versatility of a biologic system in the treatment of industrial wastes," and resulted in the construction of a few experimental sewage-feed trickling filter plants for treating cyanide wastes.

The British work convinced the American engineers that the inorganic cyanides were amenable to biologic treatment methods which would be more economical than the present chemical ones. The purpose of their laboratory work at Pennsylvania State University in Lancaster was to gain basic metabolic data on the microbiologic processes and to learn if the cyanide can be metabolized without feeding sewage into the system. They began with a culture of sewage organisms (an activated sludge from a college sewage treatment plant) as the source of the richly varied bacterial flora they would need. They acclimated the sludge by gradually substituting cyanide and nutrients, until a flourishing culture was obtained which was relying on cyanide exclusively for its carbon and nitrogen (no more sewage had to be fed).

One of the systems they developed metabolized over 99 percent of the cyanide, converting 97.9 percent of the cyanide carbon to harmless CO_2 gas, and 90 percent of the cyanide nitrogen to ammonia, nitrite, and nitrate.

Authors of the study were John Nesbitt of the Pennsylvania State University in Lancaster, Robert Kohl from Gilbert Associates, Cleveland, Ohio, and Elmer Wagner of Huth Engineers in Lancaster.

Sterility in lead-exposed women explained by study of effect on monkey ovary

The damaging effects of lead on female reproductive functions have given rise to laws protecting women in occupations with lead hazards. Women exposed to lead show disturbances of menstruation and periods of sterility. If pregnancy does occur, the chances of miscarriage are increased. Children born are apt to be weak, sickly, and slow to develop. Those who survive may be mentally retarded.

Gertrude J. Vermande-Van Eck and J. Wister Meigs at Yale University, New Haven, Conn., chose the rhesus monkey for studies of the effects of lead on the reproductive system. The similarity of human and rhesus ovaries and of the cycle of ovulation (the 28-day duration, with one egg per cycle ovulated on day 11–16, and the similar cyclic bleeding and vaginal changes) suggested that results in the monkey would have significance for humans.

With weekly injections of lead chloride, the same clinical and laboratory symptoms developed in all 11 monkeys that are commonly seen in human industrial lead intoxication. Urinary lead rose very high, beginning within 48 hours. The familiar "lead line" of bluish-gray lead sulfide deposits on the gums appeared after 3 or 4 months. Weight dropped, hypochromic anemia developed, and 1 of the 11 developed neurologic symptoms (paralysis).

The menstrual periods ceased after an average of 2 months and virtually all signs of other ovarian influences (in sex, skin color, and swelling) had disappeared after 8 months of injections.

One ovary was removed from each monkey and examined at 8 months (the peak of lead intoxication). These ovaries were abnormally flat and white, showing no ripening egg follicles. Microscopic examination showed degenerating germ cells and encroachment of connective tissue throughout the organ.

The monkeys were then allowed to recover, and after 8 months without lead injections, the other ovary was removed. It was found normal, both grossly and microscopically, with normally developing egg follicles. Recovery was general when the lead injections were stopped. Gum lead line disappeared, anemia improved rapidly, weight increased, and normal menstrual periods and other gonadal functions returned in 1 to 5 months. Microscopic examination of kidneys showed very little evidence of damage at the end of the study.

One interesting finding was that orally administered lead did not seem to be absorbed. None appeared in the urine and no symptoms of intoxication developed from it.

Regarding the ovarian changes, the investigators summarize, in "Fertility and Sterility": "The results support clinical observations of menstrual abnormalities in women exposed to lead. It was evident that our animals were unable to conceive, and it is likely that the sterility found in lead-exposed women has a similar origin."

Urinary coproporphyrin test for screening lead poisoning suspects

A simple qualitative technique for rapid clinical urine coproporphyrin estimation, has proven reliable and sensitive as a screening test in 258 Baltimore children in whom lead poisoning was suspected. The chief value of the test is its ability to disclose those patients in whom brain damage may be imminent from large amounts of ingested lead, but who do not give a clear diagnostic picture of lead poisoning. The test was uniformly positive in such patients in the Baltimore series, whereas other quickly available ancillary methods were not.

This is reported from the Johns Hopkins University School of Medicine and Hospital, and the Baltimore City Hospitals, Baltimore. Philip F. Benson, now at Guy's Hospital, London, and J. Julian Chisolm, Jr., of the Baltimore City Hospitals, report the techniques and the results of its laboratory and clinical evaluation, in the Journal of Pediatrics.

Derangement of porphyrin metabolism, associated with increased urinary excretion of coproporphyrin, is an early and constant finding in lead intoxication. Early diagnosis and treatment are important for preventing the brain lesions of severe lead poisoning and the consequent high risk of neurologic disorders and death.

The technique involves extraction of the urine in ether and hydrochloric acid. The coproporphyrin concentration of the sample tube is estimated by its fluorescence intensity as compared with that of a standard tube. Results are expressed on an arbitrary scale ranging from 0 to ++++ (as 0 or + for normal, ++ for slight elevation, and +++ or ++++ for marked elevation indicating dangerous amounts of lead in the tissues). The technique is said to be easily acquired and to take only a few minutes. The apparatus and reagents are readily available to physicians.

Find role for sympathetic nervous system in carbon tetrachloride toxicity

The characteristic liver damage of carbon tetrachloride poisoning may result, not from direct injury to the tissues, but indirectly from their oxygen starvation. Evidence is presented that this oxygen deprivation is caused by stimulation of the central sympathetic nervous system, leading to restriction of blood flow to the liver. These are results of studies by Theodore M. Brody, Deane N. Calvert, and Kenneth E. Moore at the University of Michigan, Ann Arbor.

The liver damage of excessive exposure to carbon tetrachloride and related halogenated hydrocarbons has been a major cause of industrial poisoning, and the mechanism of the poisoning has been a subject of extensive research for many years. Two very different concepts of the mechanism of toxicity have arisen. One holds that the chemical produces the damage indirectly by causing swelling of liver cells, cutting off the tissue oxygen supply. The other more recent line of reasoning suggests that it directly attacks the mitochondria of the liver cell, leading to loss of enzyme activity vital to the tissues.

The Michigan investigators present evidence that carbon tetrachloride and related chemicals may produce the liver damage indirectly by acting on the central nervous system with a prolonged rise in central sympathetic outflow reinforced by epinephrine release from the adrenal.

They report that experimental stimulation of sympathetic nervous supply to the liver can cause restriction of blood flow and tissue damage in the liver. Further, stimulation of the sympathetic nerve supply to fat depots causes a release of unesterified fatty acids and subsequent fatty deposition in the liver, as occurs in carbon tetrachloride poisoning. Conversely, sectioning of the spinal cord, adrenergic blockage, and other maneuvers to modify the effects of sympathetic stimulation, can modify some of the liver changes typical of toxic dosage of carbon tetrachloride in the rat.

These and other findings implicating the sympathetic nervous system are reported in three papers in the American Journal of Physiology.

Trout accumulate chromium contaminating their waters at sublethal levels

Although chromium contamination of water is known to be toxic to important food and game fish, past fish studies have been limited to the determination of lethal doses, and little is known of the effects of exposure to sublethal levels. From such a study in rainbow trout, J. Knoll and P. O. Fromm of Michigan State University in East Lansing report that these fish can accumulate chromium in several organs to levels above the environment when exposed to 2.5 milligrams per liter of water, a relatively low level of environmental contamination.

Chromium is of long-range significance as a pollutant of streams, lakes, and potable water supplies, due to waste disposal by industry. Considerable amounts of the metal in its hexavalent form are often present in the environment of fishes.

The chromium accumulation measured in the trout by the Michigan investigators occurred in the spleen, posterior gut, pyloric caeca, stomach, liver, and kidney. The amount accumulated in muscle, the edible part of the fish, was insignificant, indicating that human consumption of rainbow trout taken from waters contaminated with chromium at levels no greater than 2.5 milligrams per liter would probably present no serious human health hazard.

The Michigan study was reported in Physiological Zoology.

Toxic nitrogen dioxide gas in farm silos as extensive health hazard for farmers

The occurrence of nitrogen dioxide gas in farm silos has only been reported within the last decade, and has been increasingly implicated in deaths and serious incapacitation among farmers. It is now regarded as a definite farm occupational hazard.

The seriousness of the hazard has been indicated by a DGMS-aided statewide survey in Minnesota. As part of the survey, 332 individual farm silos, and factors associated with the preparation of their silage, were subjected to detailed study by J. V. Scaletti, C. E. Gates, R. A. Briggs, and L. M. Schumann of the University of Minnesota, St. Paul.

Forty-two percent of the silos showed concentrations of nitrogen dioxide considered to be hazardous (exceeding 4 parts per million of air). Studies of related agronomic practices and conditions showed that the greater the amount of organic matter in the farm soils at the time the silage crop was prepared, the greater the number of positive tests for the gas in silo air. Significant, through weaker, correlations with levels of available potassium and phosphorus in the soil were also recorded.

Use of sodium metabisulfate as a silage preservative seemed to be associated with a reduced occurrence of the hazard. (Only 1 of 21 silos containing this chemical showed evidence of nitrogen dioxide production.)

The exact relationship of the gas production to the factors found associated with it is not yet known—the study was preliminary and exploratory. The findings are published in the Agronomy Journal.

Patterns of child injury in car accidents reported from study at Cornell

A biostatistical study by Cornell University of the measurable consequences of automobile accidents has revealed a pattern of injury for exposed children which differs from that for exposed adolescents and adults. Fifty-two percent of exposed children (under 12 years) were hurt, compared with 71 percent of exposed adolescents (12 to 18 years) and 80 percent of adults. The multiplicity of injuries also increases with age, children averaging 1.4 body areas involved, adolescents 2, and adults 2.2. Head injuries were more frequent in children, injuries to other body areas less frequent.

The injuries are milder for children when they occur in the head, neck, thorax, and abdomen. Their lower extremity injuries are more severe.

In each seating area of the car, injury increases with increasing age. In each age group, injury associates with seat area occupied; rear seats are safest (frequency and severity of injury are lowest). "Unusual" seating appeared to be more dangerous than either front or rear seating in the usual arrangements. ("Unusual" is an omnibus category including persons standing, reclining, lap-carried, fourth occupants of three-occupant seats, occupants of center-bank seats in station wagons. etc.)

The data of this study were drawn exclusively from nonpedestrian accidents of passenger cars, occurring on rural and open highways, and involving injury to at least one occupant. Altogether, 14,520 cars, 31,925 exposed occupants, and 23,475 injured occupants of known age were considered in the study.

The Automotive Crash Injury Research of Cornell University, New York City, is sponsored by research contracts with the Department of the Army, supplemented by grants from the NIH Division of General Medical Sciences. The data were collected by John O. Moore, Boris Tourin, John W. Garrett, and Robert Lilienfeld of the Cornell staff, with the collaboration of physicians, public health workers, and investigating officers working the States.

The results of the study on child injuries were announced in part during 1959 at the 14th International Conference on Pediatrics, Montreal, Canada, and at the annual convention of the Florida Society for Crippled Children, Palm Beach, Fla. A paper describing the completed work was made available to DGMS in 1960.

FINDINGS PERTINENT TO CLINICAL MEDICINE

Advantages of saline over blood for replacement of fluid in shock from burns

Impressed by the burden of residual effects of present burn treatment methods, Ben Wilson and Jerry Stirman of Southwestern Medical School, Dallas, Tex., have sought modes of burn treatment which are comparable in simplicity and reversibility to the derangements they are intended to remedy. They emphasize that the early life-threatening tendency to acute fluid volume loss and circulatory failure (shock) in burns is a passing phase, and that a mode of treatment should be used which compensates this loss only during the time it threatens recovery. Thus the preferred medium for expanding diminished fluid volume in burn shock would be solutions of physiologic salts, given orally or intravenously, rather than transfusions of whole blood, which has effects lasting beyond the transient crisis of shock.

The evidence reinforcing this philosophy was obtained in an analysis of records of 430 patients, treated for burns within 48 hours, with or without the use of whole blood. The reported findings seem to confirm that the simplest and safest available modality for routine treatment of burn shock is saline resembling the blood in salt composition, taken by mouth according to the need expressed by the patient.

The chief complications which prevented satisfactory oral voluntary use of saline in the Dallas study were inability of the patient to communicate and cooperate (as in unconsciousness), acute stomach dilatation (which contributes its own component of circulatory collapse to that of the burn shock), and acutely elevated body temperature (which also adds separately to circulatory collapse, especially when compression bandages are used in hot weather). The Dallas investigators suggest that under these circumstances, saline be administered intravenously as necessary to make up the loss, and attempts be made to relieve the complicating conditions. (Stomach dilatation is successfully relieved by stomach tube, and overheating by ice packs.)

The investigators acknowledge the existence of circumstances, uncommon in their study population, in which the use of other volume expanders than saline may be preferable in treating burn shock. Infancy, and the severe protein depletion of starvation were mentioned as such circumstances.

For the Dallas study population, cases of first-degree burn, and burn involving less than 15 percent of the body were excluded from the data, because these cases were not considered to require replacement of fluid volume. Cases with more than 65 percent of the body surface burned, and those over 61 years of age were also excluded, because their expected mortality approached 100 percent, according to the analytical method they applied to the data (Bull and Squire's profit analysis).

When cases from the study population were grouped according to the two modes of treatment (volume replacement by saline only, versus volume replacement by whole blood plus saline) and according to percentages of body surface burned, the data showed that the deaths which occurred within the first 10 days were limited entirely to the group which had received whole blood. Analysis of mortality data for all the subjects whose burns covered 30 to 44 percent of the body surface showed a 27-percent mortality rate for those receiving whole blood during their initial treatment, and only 4 percent for those who had received only saline. For those with 45 to 64 percent involvement of body surface, an 89-percent mortality is reported for those treated with whole blood, while the "saline only" group showed a mortality rate of 36 percent. This difference is described as highly significant, indicating that a balanced salt solution can be used effectively and safely in extensive burns as well as those involving only limited areas of the body.

A similar experience with mortality difference for the two kinds of therapy was found when mortality was correlated with depth of burn, as well as extent.

Experimental and clinical studies indicating cause of death (usually respiratory failure) following inadequate treatment of burn shock are also presented by the Dallas team. Other treatment formulas, derived from their experience and philosophy of burn management are also suggested by the investigators in their report in the Journal of the American Medical Association. Detail as to preparation and administration of salt solutions for oral and intravenous use; and suggestions concerning management of exceptional cases, pain, contractures, and wound debridement and care are included.

Fetal eggs enable inborn heart disease diagnosis before birth

Saul D. Larks and coworkers at the University of California have shown in the past 2 years that the fetal electrocardiogram (ECG) becomes large and clear at about the 20th week of pregnancy, and that it is useful for the diagnosis of multiple pregnancies.

Larks, and Lawrence Longo, now report in the Journal of the American Medical Association, recognition of congenital heart disease before birth in four infants by this method. The ECG's showed three of the infants to have interrupted conduction of heartbeat from atria to ventricle (heartblock). In the fourth(abnormal prenatal ECG was shown at death (5 days after delivery) to be due to a coarctation, or constriction, of the aorta.

Prenatal diagnosis could prove a lifesaving advance in diagnostic ability; for some of the cases may be correctable surgically. It may also be possible, with the aid of the fetal ECG, to determine precisely when the congenital malformations arise and thus to relate their occurrence to suspected causes, such as maternal infections.

Urge concept of essential fatty acids as food to be included in balanced diet

Public and professional interest has centered for some time on the role of the saturated and unsaturated dietary fatty acids in health and disease, especially regarding the diverse effects of these two groups of dietary lipids on the blood lipids, in connection with atherosclerosis.

The suggestion now has been made that the essential unsaturated fatty acids have important functions in fat transport, that excessive feeding of saturated fat may lead to deficiency of the essential unsaturated, and that the concept of a balanced diet should be enlarged to include consideration of the balance of essential versus nonessential fatty acids.

"In the interests of preventive medicine, a plea is made for the nutritional rather than therapeutic approach to the problem of providing sufficient essential fatty acids for maintenance of normal health. That is, essential fatty acids should be considered food rather than medicine."

These are the concluding lines of a paper on "Essential Fatty Acids in Nutrition and Metabolism" by Ralph T. Holman in the A.M.A. Archives of Internal Medicine. Holman is professor of Physiological chemistry at the Hormel Institute, University of Minnesota, Austin, Minn.

From one line of investigation Holman learned that certain tissues (heart and testis) show dramatic changes in fatty acid constitution on an EFA-deficient diet, and that those changes can be made to occur much more quickly and drastically (at least in testis) if any of several techniques for raising the blood lipids are applied simultaneously. Depletion of the polyunsaturated fatty acids of the tissues to the point of their actual degeneration was possible only by the combining of dietary cholesterol or hydrogenated fat with EFA deficiency.

"These results suggest that influences which elevate plasma cholesterol deplete the animal of his store of polyunsaturated fatty acids and thereby hasten EFA deficiency," he summarizes. "If this be the case, then polyunsaturated fatty acids (including EFA) are necessary for the normal transport of cholesterol and plasma lipids. This function of EFA probably would require much larger amounts of EFA than does the maintenance of normal tissue without the stress of excessive lipid transport."

Holman also reports studies showing that "despite radical changes in dietary fat, the cholesterol and polyunsaturated acid contents of the plasma remained rather constant." He interprets this to mean that the EFA required for fat transport in the blood tend to be maintained in the blood even at the cost of the EFA in the tissues. "Prolonged feeding of a saturated fat could therefore lead to a depletion of stores of unsaturated acids and a chronic EFA deficiency," he summarizes.

Evidence of a fundamental need within the cell itself for adequate and balanced supply of these unsaturated fatty acids is presented from studies at the level of enzymatically active subcellular particles, by Holman and others. Evidence is included of the existence of large proportions of the polyunsaturated acids in the enzymatically active particles of beef heart, and of rapid depletion of these substances in subcellular particles when a fat deficient diet is fed. "The changes in polyunsaturated acid composition takes place several weeks before deficiency symptoms appear, suggesting that a primary metabolic lesion is the first result of deficiency," Holman explains. The evidence suggests the easily oxidized unsaturated and essential fatty acids may function as active centers in enzyme structures important in actively metabolizing tissues.

"The essential fatty acids are found abundantly in nature and can readily be obtained in foods on the market," he suggests.

"A wise selection of foods for a balanced diet will provide adequate amounts of essential fatty acids. However, the concept of the balanced diet must be enlarged to include consideration of the balance of essential versus nonessential fatty acids."

Cornell team, Division of Indian Health and DGMS in study of Navajo medicine

A joint medical-anthropological research program on the health of the Navajo is being carried out by Cornell University investigators. They are studying the patterns and socioeconomic aspects of disease, the training of Navajos as medical aids, and relationships between physicians and medicine men.

Walsh McDermott, Kurt Deuschle, John Adair, Hugh Fulmer, and Bernice Loughlin, of the New York Hospital, Cornell University Medical Center, New York City, are conducting the study in cooperation with the Division of Indian Health, PHS. The broad cross-cultural program of work was begun in 1956 to investigate the influence of new types of medical technology. Preliminary findings have been reported in two consecutive issues of Science and in the American Review of Respiratory Diseases. The Navajo Tribal Council also shares in the financial support, which derives partly from a DGMS research grant.

The total program of the Cornell project consists of three large general studies and a number of smaller, segmental, and more sharply defined studies.

The first of the three is a socioeconomic study of the community as a whole, with special attention being given to factors pertaining to health and disease. This has brought out the particularly high birth rate among the Navajo, a finding which has bearing on estimating future health and educational needs. In a 3-year period, the net gain in population in the group of approximately 2,000 was 239 persons.

The second general study concerns defining the pattern of disease in the community. Complete physical examinations and laboratory studies were carried out. In the first 1,600 persons examined, 76 percent of the disease present was microbial in origin. There were also cases of trachoma, and congenital hip disease was extraordinarily prevalent. Although tuberculosis was fairly widespread, the incidence has fallen substantially during the 3-year period. Streptococcal infections and measles appeared to be more serious in Navajo society than in non-Indian.

The third study involves the training of Navajo men and women with limited schooling as field auxiliaries to the public health nurses. Known as health visitors, these subprofessional workers help the field nurse and often serve as driver-interpreters, sanitarians, and community workers. Three or four health visitors generally assist each public health nurse. The social scientists of the project are studying the relationships between the Navajo health visitors and the community and between the health visitors and the professional staff.

An example of an unexpected cultural barrier faced by the Cornell scientists was the fact that in Navajo society, congenital hip disease is considered neither a disease nor a particular disability. Surgical fusion of the hip joint, as practiced in children in non-Indian society for prevention of a more serious handicap in years to come, complicates the life of the Navajo child for he is then unable to sit easily on the floor or to ride horseback. Rather than improving his lot, modern surgery, in such instances offers no obvious advantages. The Cornell staff is making a genealogic study of the disease, hoping to establish in which families it has existed in the past. Diagnostic X-rays will then be used on infants born to those families, so that the disease will be caught early enough and surgery can thus be avoided.

In one of the segmental studies, Dr. McDermott and his staff are seeking to learn the extent to which an uneducated nonliterate people can assume responsibility in daily self-administration of drugs, such as is necessary in treating tuberculosis. It has been found that approximately 15 percent of the group are unreliable on this score.

In other studies, careful translation of medical and disease concepts is underway. In this regard, social scientists are studying the relationships between physicians and the Navaho medicine men. These relations have been found good, and the medicine men recently have been referring some of their patients to the physicians for advice and treatment.

The Cornell investigators point out that the introduction of any new technology into relatively primitive societies must be undertaken with caution. They are attempting to determine the rate at which new medical concepts can be introduced into the Navaho culture.

Evidence opposes routine whole blood transfusions during gastric operations

Opposition to widely advocated practices of routine and prophylactic transfusion of whole blood, particularly during gastric surgery, is expressed in a report by surgeons at the University of Texas, Dallas, Tex. Drawing on a DGMS-aided study in patients undergoing surgery for benign gastric diseases, they conclude that "routine whole blood transfusions during gastric operations are not necessary."

Ben J. Wilson and Kenneth O. Adwan present a variety of experimental and clinical evidence in opposition to the following generalizations concerning blood transfusion, which are commonly found in the literature and thought to be reflected in the practice of surgery.

1. That knowledge of blood loss during operations, as available in the literature, offers a practical basis for planned transfusions during operation.
2. That circulatory collapse often accompanies major operations and whole blood should be replaced during operation because it is much simpler to prevent shock than to treat it after it has occurred.
3. That giving blood to a person in anticipation of subsequent hemorrhage will protect him from the effects of that hemorrhage.
4. That failure to replace blood loss retards the patient's convalescence, and that replacement is more effective when whole blood is given as the loss occurs.
5. That the loss of oxygen-carrying red cells that accompanies blood volume loss imposes a burden on recovery that cannot be effectively compensated by replacement with any non-red-cell containing fluid.

The detail of the evidence presented in refutation of each of these assumptions may be seen in the AMA Archives of Surgery. The evidence was accumulated from various sources during a period of more than 9 years' clinical and experimental study of the effects of hyper- and hypovolemia.

A DGMS-aided study of 100 consecutive patients undergoing subtotal gastrectomy for benigh ulcers at Parkland Hospital, Dallas, affords some of the evidence. For this group, whole blood during their surgery was withheld until there were clear indications of threat from anemia. (Only 2 of the 100 patients received any whole blood during surgery.) This group was compared with a like series of 99 gastric surgery cases at the Dallas VA hospital who were similarly treated, except that they received blood transfusions 10 times as frequently during operation (22 of the 99 received whole blood during operation).

The reported difference in morbidity and mortality between the two groups was slight. "It would appear from this comparison that failure to replace whole blood losses during operation is not detrimental," Wilson and Adwan write.

They also summarize the results of experimental studies in which survival of animals transfused with compatible whole blood prior to a standardized hemorrhage, was compared with that of controls not transfused prior to the hemorrhage. Only 15 percent of the transfused animals survived, compared with 75 percent of the controls. These and other findings were interpreted as evidence that such transfusion in the absence of an existing physiological need for blood, may add to risk of morbidity and mortality from gastric and other operations.

The Dallas investigators acknowledge that whole blood transfusions are indispensable for treating large blood losses that are inimical to recovery. They suggest maximum discrimination in the selection of such cases, and care in weighing the risks of giving blood against those of not giving it.

Serum folic acid assay by cheese bacteria valuable for diagnosis of anemia

Lactobacillus casei, a folic acid-dependent organism common in cheese, is reported capable of using human blood serum as its sole source of this vitamin. The New York City group which reports this finding has developed an assay method based on the growth of this organism in serum samples for use as a diagnostic aid in singling out the cases of megaloblastic anemias which are due to deficiency of folic acid rather than of vitamin B_{12}. Sharp delineation of such cases and their effective treatment with folic acid are reported.

Earlier reports by the New York team that a folic acid-dependent organism (*Lactobacillus casei*) utilizes the folic acid activity of fasting serum for its growth were received with reservations by some authorities, for there has been doubt that the blood contains any folic acid during the fasting state. An English worker commented in the British Medical Journal that, although some growth of folic acid dependent mutants may occur, "* * * there is no evidence that this slight growth reflects the presence of folic acid in those blood samples."

The New York (Mount Sinai Hospital) group advanced their case much further in 1960, reporting that they can relate the growth of *L. casei* in sera to folic acid nutritional states and that the measure of this growth is useful in distinguishing cases of megaloblastic anemia due primarily to folic acid deficiency from those which are due primarily to vitamin B_{12} deficiency.

Nearly all of the megaloblastic anemias are attributable to deficiencies of either vitamin B_{12} or folic acid or both. Delineation of those due to B_{12} deficiency has been aided by availability of microbiologic assays for this vitamin in serum. The presumed absence of folic acid from the blood has, until now, denied the convenience of such assays to those who wish to assess folic acid nutritional status.

In the hematologic journal Blood, the New York group reports use of this assay for determination of the levels of folic acid active material in normal subjects and in 18 patients with known megaloblastic anemias. The patients included cases of megaloblastic anemia of malnutrition (3 cases), alcoholic cirrhosis (3), infancy (2), pregnancy (2), and of various gastrointestinal diseases (8). Determinations were also done on 10 normal controls, and on patients with various other forms of anemia.

Sixteen of the 18 patients with the known megaloblastic anemias were shown by the assay data to have low serum folic acid levels, according to the New York team. In all cases except one, the anemia responded to folic acid administration, and in most the recovery was complete, according to the report in Blood.

Twenty-four sera provided by another lab and representing unknown clinical states were also assayed for folic acid, and five were found low. The investigators report that in all but one, the folic acid level obtained by the assay correlated with the clinical diagnoses which we subsequently obtained.

"While it must be emphasized that the chemical nature of folic acid-active material in fasting serum is unknown," they explain, "nevertheless the quantity of this material appears to reflect the folic acid nutritional status of man."

Participants in the study were Victor Herbert, Herman Baker, Oscar Frank, Inez Pasher, Harry Sobotka, and Louis Wasserman of Mount Sinai Hospital, New York. The work was aided by an NIAMD, as well as a DGMS grant.

Dietary variations affect yield of inborn defects from vitamin E deficiency

Dorothy Wei Cheng, of the State University of Iowa, reported, in 1952, the first experimental congenital abnormalities to be produced by vitamin E deficiency. She has since announced a number of findings suggesting interaction of other physiological influences with the vitamin E deficiency in the production of congenital malformations. In 1959 her team reported DGMS-aided studies showing that the incidence of congenital abnormalities resulting from vitamin E deficiency can be reduced or abolished by treating the deficient mothers with female gonadal hormones (estrone or progesterone). Cheng's experimental animal for these continuing studies is the rat.

In 1960, Cheng's group published a report in the Journal of Nutrition suggesting that dietary constituents, apart from the known vitamin E intake, may influence the occurrence of congenital abnormalities and fetal losses induced by vitamin E deficiency. The new findings were facilitated by the use of synthetic diets, instead of the semisynthetic ones used previously. (Pure crystalline vitamins A, B, and D were substituted for the natural food materials which had been used as a source of vitamins other than E in the earlier experimental diets.) Contributing dietary factors which were previously beyond effective control thus became amenable to study.

Four diets of different composition (two synthetic and two semisynthetic) were developed and used in the study. All four were shown to be sufficiently lacking in vitamin E activity to exclude the possibility of fetal survival in any female rats limited to these diets. (In control studies, 100 percent of the young conceived in females on these diets were found to be reabsorbed.) The diets were then supplemented during pregnancy with just enough vitamin E to maintain the females in a "borderline" vitamin E nutritional state, sufficient to alter normal development of their young without causing their prenatal death.

Twenty different types of congenital abnormalities are listed as resulting from such treatment. These included malformations of viscera, skeletal system, central nervous system, circulatory system, and mouth.

Varying the composition of the diets influenced the yield of abnormal as well as normal young rats, the incidence of fetal resorption, and the average number of implantation sites in the uterus following conception, the investigators report.

Doubling the "borderline" allowance of vitamin E (alpha tocopherol) supplementation during pregnancy resulted in a uniformly significant increase in the percentage of normal young delivered, but even with this doubling of vitamin E allowance, the percentage of abnormal young could be significantly increased or decreased, depending on which of the four rations was used. The substitution of crude casein (milk protein) for the vitamin free casein of a synthetic diet appeared to cause a decrease in the incidence of fetal resorption and an increase in the number of abnormal young and in the number of implantation sites. This is attributed by the authors to the addition of trace vitamins (presumably other than vitamin E) which are present in the crude casein. The addition of cod liver oil to a pure synthetic ration resulted in a significant increase in the yield of normal young together with a significant decrease in the percentage of resorption.

The hope is that such studies will help expose, for preventive action, interrelated dietary and other factors which may be involved in the causes of human congenital abnormalities.

Thomas Bairnson, A. N. Rao and S. Subbammal participated with Dorothy Wei Cheng in this work.

Decline of serum vitamin B_{12} in pregnancy related to withdrawal by fetus

Bacon F. Chow and Kunio Okuda, of Johns Hopkins University, Baltimore, Md., have found that the normal fetus draws vitamin B_{12} and other nutrients such as iron and vitamins C and B_6 against a concentration gradient across the placenta with the result that higher serum levels of these substances are maintained on the fetal side of the placenta than on the maternal side. Their report appeared in the Journal of the American Medical Association.

Previous studies had shown a decline in maternal vitamin B_{12} serum levels with advancing pregnancy. The Johns Hopkins investigators demonstrated in tests on 25 women that the umbilical cord serum level of vitam B_{12} and various other vitamins rises as the result of an active withdrawal from mother to fetus. In view of this fact, it was considered helpful to know whether or not the withdrawal of B_{12} affected the mother. Although no real illness appeared in the mothers, there was biochemical evidence of B_{12} deficiency, based on erythrocyte glutathione and glucose-ribose enzyme content. In another experiment, rats on a standard diet with liver supplements were repeatedly mated. Their maternal reserves became depleted, and it was found that both the size and the number of young were reduced, with each successive pregnancy.

In 14 pregnant women, most of them in active labor, the intramuscular injection of crystalline vitamin B_{12} resulted only in a temporary elevation of the vitamin B_{12} concentration in the maternal blood above that in the fetal blood; after 6 hours the fetal levels were again higher than the maternal.

To test the nature of the selective transfer mechanism across the placenta, Drs. Chow and Okuda carried out experiments to determine whether all soluble materials could be concentrated in the fetus, in which case the transfer of B_{12} might not be particularly significant. Tests with glucose and inulin indicated that while they apparently move across the placental membrane via a process of passive diffusion they are not actually drawn across the placenta as in the case of B_{12}. The concentrations of glucose and inulin adjusted to the same levels in the serum of both mother and fetus.

According to the investigators, a factor that points to the physiological importance of the differences in the vitamin B_{12} serum gradient is that in cases of cretinism, the B_{12} concentration in the umbilical cord blood of the cretins is low. This may indicate that the mechanism of transfer of B_{12} from mother to fetus in cretins is not functioning correctly. Further study is required.

Starvation may prolong drug action by slowing liver enzyme activity

The ability of mammals to metabolize drugs appears to reside largely in the enzymes of the liver cell associated with the endoplasmic reticulum from which the microsomal fraction is derived. Starvation-induced changes, occurring in the endoplasmic reticulum, led a team of pharmacologists at Iowa University to look for corresponding changes in drug metabolism. They now report evidence of marked slowing of drug oxidation along most of a variety of metabolic pathways studied in starved animals.

The Iowa City team used mice for in vivo and in vitro studies of starvation effects on the side chain oxidation pathway of hexobarbital, N-dealkylation of pyramidon, hydroxylation of the aromatic ring of acetanilid, oxidation of the ring sulfur of chlorpromazine, reduction of aromatic nitro-group of p-nitrobenzoic acid, and reduction of aromatic azo-group of neoprontosil.

The effect of starvation in prolonging hexobarbital-induced sleep was measured in individual animals and then shown to correlate well with biochemical changes in metabolism of most of the drugs by the microsomal fraction of liver cells as determined in vitro. In other words, the animals which slept longest under the barbiturate were those whose livers were least able to metabolize most of the drugs studied. The depression of drug metabolism that occurred in most instances is attributed by the investigators to an actual loss of enzyme protein in the microsomal fraction.

In view of these findings, the nutritional status of an animal may be important in accounting for "biological variation" in drug response, according to the investigators. A properly controlled experiment should include regulation of food intake before any drug administration, they suggest. They also believe their findings may have clinical importance where drugs are administered to debilitated or malnourished patients.

Robert L. Dixon, Robert W. Shultice and James R. Fouts of the Iowa group published the data in Proceedings of the Society for Experimental Biology and Medicine.

Highlights of Progress in the Division of Research Grants 1960

Items of Interest on Program Developments

The growth, both in size and scope, of the National Institutes of Health extramural program has again necessitated expansion and reorganization of the many activities of the Division of Research Grants.

In order to coordinate the operation and policies of the complex and growing NIH programs for the suport of training of research manpower, the Division was assigned the administration of the NIH training grant and traineeship awards. Responsibilities in this area are: initial receipt of training grant applications with assignment to the appropriate Institute or Division, service as a central source of information in the training grant area and formulation of policies and procedures pertaining to training grants.

To assure maintenance of the Division's high standards of review for the growing number of research grant applications, the number of study sections in the Research Grants Review Branch was increased from 35 to 36, an advisory committee on computors was organized and the position of Deputy Branch Chief was established. The study sections, whose primary function is to provide initial review of research grant application, have also continued their program activities by stimulating and planning an increased number of meetings and institutes to exchange, gather and publish information on specific health and medical problems and needs.

The health research facilities program began its fifth year of operation in July 1960. As of October 1, 1960, 212 research facilities constructed under this program were completed and in use. These represent Federal expenditures of $28.6 million and a total construction cost of over $139 million.

The Research Fellowships Review Branch has changed the composition of its review panels so that outside specialists now review and evaluate regular fellowship applications. In the past this process has been carried out by NIH research personnel. Additionally, the number of these disciplinary review panels has been increased from 9 to 10 to help accommodate the sharp increase in the number of applications. Near the end of 1960 the entire fellowships program was modified and expanded to meet changing needs of the scientific community. As a result the Branch has been assigned new responsibilities for development of policies, rules and procedures for the senior research fellowship grants program and special fellowships grants program.

During calendar year 1960, the Division reviewed and processed approximately 16,850 research grant applications requesting $338,700,000 and 4,000 applications for research fellowships. This compares with 14,841 research grant applications and 2,848 fellowship applications in calendar year 1959.

Fiscal year 1960 research and construction grants

The National Institutes of Health awarded 11,743 grants totaling $229,505,503, for research and construction of research facilities in non-Federal institutions during fiscal year 1960.

Approximately 87 percent of the total amount granted, or $198,719,397, went for support of 11,572 research projects concerned with major diseases and various basic problems in the medical and biological sciences. The grants were made to 973 institutions in the United States and to 145 institutions in 38 other countries.

Grants, totaling $30,786,106, to help build, equip, or expand 171 research facilities, were awarded on a matching basis to 141 institutions throughout the country.

Dr. Allen appointed Associate NIH Director for Research Grants

Dr. Ernest M. Allen, Chief, DRG and Associate Director for Research Grants, NIH, was given full-time staff responsibility as Associate Director. DRG operating responsibilities are now carried out by Dr. Dale R. Lindsay, who was appointed Chief of the Division. His assistant is Dr. Clinton C. Powell, who has been named Deputy Chief.

Dr. Lindsay, formerly Assistant Chief of the Division, has been a career officer of the Public Health Service since 1943. His first assignment in the Public Health Service brought him into malaria control in the war areas program. In 1948 he was appointed chief of the Service's field station in Thomasville, Ga., where he remained until his transfer to the Division of Research Grants in 1953 as Chief of its Program Analysis Section. Two years later he occupied the post of Scientific Director of the Division of Research Grants, and in 1957 the position was renamed as Assistant Chief.

Dr. Powell, formerly Assistant Grants Branch Chief for Clinical Research in the Division of Research Grants, is also a career officer in the Public Health Service. Prior to his Branch Chief position he served as Executive Secretary to the Radiation and Surgery Study Sections. In 1956 Dr. Powell headed the radiological health medical program, Division of Special Health Services.

Federal Aviation Agency Advisory Group

Dr. Joseph V. Michalski, Assistant Chief of the Research Grants Review Branch, DRG, accepted membership on the Research Advisory Group of the Bureau of Aviation Medicine, Federal Aviation Agency, in September.

This group reviews and evaluates medical research contract proposals submitted to the Bureau.

The group includes representatives of NIH, the U.S. Navy, Army, and Air Force, and Georgetown University School of Medicine.

DRG training grant review

DRG's Training Section began active review and assignment of all NIH graduate training grant applications to Institute training programs in July.

In February 1960 the Division of Research Grants was designated as the center for administration of NIH training grant and traineeship programs. As a result the Division established during April a new Training Section to be headed by an Assistant Chief for Training, DRG. This position was filled on April 15, with the appointment of Dr. Fay M. Hemphill, who had been serving as Chief of DRG's Statistical Design and Analysis Section. Subsequently, Dr. Roy P. Lindgren of DRG was assigned as Project Review Officer, and further staffing brought the Section up to its present complement of eight persons.

The Section's responsibilities in the training grants area parallel DRG's activities in the research grants area: receiving, assigning, and distributing applications; reviewing budget requests of applications; establishing policies and procedures for payment and management of training grants and awards; maintaining central records; establishing training grant review committees where requested; and other duties involving liaison.

Fellowships Branch revises programs

The Research Fellowships Review Branch announced the establishment of two new fellowship grant programs, career research professor and special fellowship, and the revision of a third, senior fellowship.

The career research professor grant program was established to support individuals of demonstrated capacity to pursue with distinction a professorial career in independent research and training. Grants are awarded initially for 5 years of support and are renewable at 5-year intervals. In this first year the award will be made only to schools of medicine, osteopathy, dentistry, and public health. The earliest effective beginning date is July 1, 1961.

The special fellowship grant program provides support for promising young investigators, not yet eligible for a higher level, who the applicant institution feels would be an important addition to its teaching and research staff. This grant program is in addition to the present special fellowship awarded directly to individuals for advanced or special training.

The senior fellowship grant program, formerly limited to preclinical science departments, has been expanded to include clinical departments and certain departments in university graduate schools and other institutions. This program is for the support of individuals with at least 5 years of relevant research experience beyond the doctorate, who have demonstrated high potential for a research or academic career.

Advisory Committee for Computers in Research

An Advisory Committee for Computers in Research, composed of biologists, physicists and experts in computer technology was established in DRG in September.

The committee has four general functions: (1) to advise the NIH on the role of computers in medical and biomedical research, areas of medical research in which computer usage might be encouraged through NIH efforts, and areas of research in computer technology which should be stimulated and supported by NIH activities; (2) to appraise and assign priority scores to applications for grants referred to the committee for such actions; (3) to appraise and prepare recommendations on applications and inquiries referred by study sections; (4) to stimulate use of computer techniques in medical research and development of computer technology as applied to biomedical problems.

Chairman of this new nine-man committee is Dr. Lee B. Lusted of the University of Rochester. Other members are: Mr. Paul Armer, The Rand Corp.; Dr. Mary A. B. Brazier, Massachusetts General Hospital; Dr. David Garfinkel, New York State Psychiatric Institute: Dr. George A. Sacher, Argonne National Laboratory; Dr. Otto Schmitt, University of Minnesota Department of Physics; Dr. Norman Shapiro, National Institutes of Health, Division of Research Services; Dr. Ralph W. Stacy, Ohio State University Department of Biophysics; Dr. Max Woodbury, New York University School of Engineering.

The first general meeting of the committee was held at NIH September 20 and 21.

Thirty-sixth study section established

On May 27, the Division of Research Grants received approval of the Director, NIH, for the establishment of the Division's 36th Study Section—Medicinal Chemistry.

The new study section was formerly DRG's Panel of Medicinal Chemistry Consultants. Dr. Helen Jeffrey, who served as executive secretary to the Biochemistry Study Section and to the former panel, continues in that capacity for both the Biochemistry and Medicinal Chemistry Study Sections.

Conference on "Phenomena of Tumor Viruses"

A symposium entitled, "Phenomena of the Tumor Viruses," sponsored by the Virology and Rickettsiology study section of DRG, was held in New York City in March.

Recent findings in experimentation with the tumor viruses were presented in papers read by 12 U.S. and foreign scientists, who have done outstanding work with viruses in various disciplines. Each presentation served as a basis for questions and informal discussion. General categories are properties of tumor viruses, host response, contributions of tissue culture, and ultrastructure.

Speeches by two NIH Administrators served as an introduction to the 2-day meeting. Dr. Joseph E. Smadel, Associate Director for Intramural Research, discussed the tumor virus research program, and Dr. Ralph G. Meader, NCI Research Grants Branch Chief, outlined administration of research support.

About 200 investigators actively engaged in work with tumor viruses participated in the meeting, supported by a research grant from the National Cancer Institute.

Dr. J. W. Beard, Duke University, was chairman of the symposium.

Conference on "Problems in Toxicology"

DRG's Toxicology Study Section, in cooperation with the Food Protection Committee and the Toxicology Committee of the National Research Council, cosponsored a symposium on "Problems in Toxicology" in Chicago.

The symposium was an intersociety meeting held in conjunction with the annual meeting of the Federation of American Societies for Experimental Biology.

The purposes of the symposium were to attract graduate students to toxicology, to encourage competent investigators to undertake research in his field, and to discuss the ever-increasing number of problems in this area.

Leading scientists talked about relatively new challenges in the field, such as "Radioactive Materials," "Submarine Hazards," "Space Hazards," and "Man-Made Noxious Environment." Other topics were "Food: Additives and Natural Components," "Drugs and Cosmetics," "Agricultural Chemicals," "Water and Atmosphere," "Recognition of Toxicology as a Scientific Discipline," and "Training of Toxicologists."

Chairman of the morning session of the daylong symposium was Dr. Chauncey D. Leake, professor of pharmacology, Ohio State University. Dr. W. Henry Sebrell, Jr., director of the Institute of Nutritional Sciences, Columbia University School of Public Health and Administrative Medicine, chaired the afternoon meeting.

Advisory Committee for Science Exposition

Dr. Ernest M. Allen, DRG Chief, is serving on a committee of advisers to the Commissioner for the U.S. Science Exhibit, Century 21 Exposition, to be held in Seattle in 1961.

The group, called the U.S. Science Exhibit Advisory Committee on Scientific Theme, Content, and Presentation, is composed of nine experts in the field of science and mass communications. This body makes recommendations on specific exhibits and methods of presentation, scientific integrity of the exposition, and overall theme.

Also serving on the committee are representatives of the Department of Defense, National Bureau of Standards, American Association for the Advancement of Science, Department of Agriculture, Harvard University Observatory, National Science Foundation, University of Pennsylvania Museum, and National Aeronautics and Space Administration.

Two Symposia on Nutrition

The DRG Nutrition Study Section cosponsored two symposia, "Problems of Nutrition Appraisal of Mankind," and "Interaction of Mineral Elements in Nutrition and Metabolism," in Chicago. The sessions were held in conjunction with the annual meeting of the Federation of American Societies for Experimental Biology.

The morning symposium, "Problems of Nutrition Appraisal," was cosponsored by the Interdepartmental Committee on Nutrition for National Defense. Investigators representing the fields of medicine, anthropology, and biochemistry conferred on "Problems of Physical Appraisal," "Dietary Appraisal," and "Problems of Biochemical Appraisal of Nutritional Status." Dr. John B. Youmans of the Surgeon General's Office, U.S. Army, served as chairman.

Papers given in the afternoon symposium, "Mineral Element Interaction," illustrated the close interrelationship of mineral elements in the living animal body. The American Institute of Nutrition cosponsored this meeting, chaired by George K. Davis, professor in the Department of Animal Husbandry and Nutrition of the University of Florida. Topics explored were calcium and phosphorus interactions in nutrition and physiology, nutritional interactions in zinc and calcium, magnesium requirement and its relation to other dietary constituents, metabolic relations of manganese to other minerals, interrelationships of iron and copper in the nutrition and metabolism of animals, and interrelations of copper, molybdenum, and sulfate sulfur in nutrition.

Fourth conference on research needs in tropical medicine

The fourth conference on research needs in tropical medicine was held at the School of Medicine, Louisiana State University in New Orleans. Similar conferences in this field were sponsored by the predecessors of the Tropical Medicine and Parasitology Study Section in 1951, 1953, and 1954.

Chairmen of the fourth conference were Dr. Stanley B. Freeborn, Chairman of the Tropical Medicine and Parasitology Study Section, and Dr. William W. Frye, vice president of Louisiana State University and dean of the School of Medicine.

The purpose of the informal, invitational conference was to explore the status of research in tropical medicine, with emphasis on the interdisciplinary areas, to better understand the current needs in the wide scope of tropical or geographical medicine; to broaden the concept of tropical medicine to geographical medicine (which includes all disciplines in addition to infectious and parasitic diseases; and to better orient subsequent research in geographical medicine.

Many of the participants were PHS grantees or potential grantees. Participants represented universities, leading pharmaceutical laboratories, laboratories of private foundations, private research institutions, World Health Organization, International Cooperation Administration, U.S. Department of Agriculture, the U.S. Army, Navy, and Air Force, Veterans' Administration, and the Public Health Service.

The program was composed of three panels: "Tropical or Geographical Medicine," "Impact of Modern Instrumentation on Medicine in the Tropics," and "Critical Problems Needing Investigation in Some Fields of Medicine in the Tropics." It was designed to encourage questions and informal discussion following the presentation of each topic. Some of the topics considered were: tropical pathology; clinical periodontal, neurological, nutritional, cardiovascular, infectious and parasitic diseases; population limitations; cancer; mental health; microbiological techniques and electron microscopy; zoonoses; immunology and fluorescent antibody techniques; biochemistry; and histochemistry. Some 15 other subjects were suggested but not included due to the lack of time; thus, a fifth conference has been recommended for 1961.

The fourth conference was supported in part by a research grant awarded to the Louisiana State University (Dr. William W. Frye, principal investigator) by the National Institute of Allergy and Infectious Diseases. Dr. Ernestine B. Thurman serves the Tropical Medicine and Parasitology Study Section as executive secretary.

Proceedings of the conference were published in September.

Genetics Study Section sponsors three symposia

The DRG Genetics Study Section sponsored the first in a series of three symposia on "Methodology in Genetics" at the University of Utah, Salt Lake City.

A recent survey by the study section indicated a critical lack of information and communication concerning current methods in rapidly advancing areas of medical genetics. These symposia bring such information up to date and will make it readily available to the genetics research community through low-cost, widely distributed publications. The meetings are supported by a grant from DGMS.

The first symposium, concerning human genetics, featured papers by 15 outstanding geneticists. The subject groupings of these papers were "Analysis of Human Heredity." "Genetics and Disease," "Mutations in Human Population," "Cytogenetics," and "Biochemical Genetics." Each group of papers was followed by an informal discussion. The second symposium, "Methodology in Mammalian Genetics." was held at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.

Thirteen papers were presented on various problems such as "Genetics Stocks and Breeding Methods." "Radiation Genetics," "Physiologic Genetics," "Biochemical Genetics," "Immunogentics," "Host Parasite Relationships," and "Somatic Cell Genetics."

The third meeting, "Methodology in Basic Genetics," will be held at the University of Texas, Austin, on May 4 and 5, 1961. The study section plans to distribute the publication of proceedings from the first symposium at this third meeting.

Summer institute in biophysical science

The Biophysics and Biophysical Chemistry Study Section, DRG, sponsored a "Summer Institute in Biophysical Science" at Massachusetts Institute of Technology.

College undergraduates, majoring in chemistry, physics, mathematics, biology or in premedical studies, attended the Institute as representatives of 16 universities and colleges throughout the Nation.

The purpose of the 2-week program was to stimulate and encourage participation in the development of the broad field of biophysics. Lectures on biophysics, a talk on "Education and Career Opportunities in Biophysics," laboratory tours and a trip to the Marine Biological Laboratory at Woods Hole, were included in the 2-weeks program.

Conference on prosthetic valves for cardiac surgery

DRG's Surgery Study Section sponsored a "Conference on Prosthetic Valves for Cardiac Surgery," at the Edgewater Beach Hotel, Chicago, Ill. The conference was supported by a grant from NHI.

Introductory remarks to the 2-day session were made by Dr. James Watt, Director of NHI. Almost 30 professional papers were presented by United States and Canadian heart specialists, including several from NHI. A discussion, led by an expert in the field, followed each group of papers, arranged in such topics as "Physiology of Valve Function." "Myocardial Metabolism," "Materials, Designs, and Testing Methods," "Replacement of the Mitral Valve," and "Replacement of the Aortic Valve."

Conference on the physiological aspects of water quality

DRG's Environmental Sciences and Engineering Study Section sponsored a "Conference on the Physiological Aspects of Water Quality" in Washington, D.C.

The 2-day program was divided into a general session, "Session on Minerals and Trace Elements," "Session on Insecticides and Organics," and a review session. The general session included discussions on "The Need for Water Quality Criteria" and "Detection and Analysis of Chemistry in Water."

The review session included summaries on minerals and trace elements, insecticides, organics, "National and International Standards of Water Analysis," and a conference evaluation.

About 65 scientists, representing Federal agencies, State health departments, universities, and private organizations throughout the United States, participated in the Conference.

Revision in procedure for grant payment

NIH 1961 grants, with certain exceptions, will be paid in four installments.

The NIH grant payment procedure was changed, as of July 1, to minimize excessive cash balances in the accounts of grantee institutions in proportion to their current operating needs.

Alma maters of principal investigators

A tabulation of the alma maters of 1,900 NIH-supported principal investigators shows that the grantees obtained their bachelor's degrees from 362 universities representing every State in the Union except Nevada.

The study, made by DRG's Statistics and Analysis Branch, was limited to investigators who received research grants in fiscal year 1960, and who attended institutions located in the United States and Puerto Rico.

The institution graduating most grantee principal investigators was the University of California, followed by Harvard, Chicago, City College of New York, Minnesota, New York University, Columbia, Yale, Michigan, Illinois, and Cornell.

Principal investigators on teaching staffs

A study conducted by DRG's Statistics and Analysis Branch reveals that of the principal investigators receiving their first research grant in fiscal year 1960, 80 percent were on the staffs of schools and universities.

Ten percent were on hospital staffs and the remaining investigators were affiliated with other types of institutions.

The tabulation also shows that of the 80 percent in schools and universities, three-quarters hold rank as assistant, associate, or full professors.

Birthplace of grantee investigators

A recent study on the birthplace of some 1,400 principal investigators receiving their first research grant in fiscal year 1960 reveals that 21 percent were born in foreign countries.

The study, conducted by DRG's Statistics and Analysis Branch, also shows that 12 percent of these 1,400 investigators are not U.S. citizens.

Other study findings indicate that 40 percent of the native-born new principal investigators were born in New York, Illinois, Pennsylvania, California, or Massachusetts. Two and one-half times as many were born in New York as in Illinois or Pennsylvania—States rated second in the above list.

Financial aid to students increases

Although college tuition costs have risen sharply during the past few years, there has also been an increase in organizations providing financial aid to students.

The Statistics and Analysis Branch, DRG, found that 86 percent of NIH's fiscal year 1960 principal investigators aged 30 or younger obtained some formal support (U.S. Government assistance, university scholarship, etc.) during their predoctoral work. Only 40 percent of those 60 or older had had formal support. For other age groups, the proportions obtaining formal educational support were: Aged 30 to 34, 81 percent; aged 35 to 39, 69 percent; aged 40 to 44, 67 percent; aged 45 to 49, 62 percent; aged 50 to 54, 54 percent; aged 55 to 59, 53 percent.

NIH researchers widely experienced

More than 25 percent of some 1,400 principal investigators receiving their first NIH research grant award in fiscal year 1960 have served in the past as assistants on research projects supported by NIH. Two-fifths of the group have been principal investigators for research projects sponsored by other agencies or institutions.

The Statistics and Analysis Branch, DRG, reports that the new investigators receiving support from the National Institute of Arthritis and Metabolic Diseases, as a group, had the widest experience in formal research projects. Almost three-fourths participated previously in sponsored research. In the comparatively new field of dental research almost 50 percent of the new investigators have participated in sponsored research as principal investigators or assistants before obtaining NIH support.

Dr. Allen addresses Rocket Society Conference

Dr. Ernest M. Allen, Chief of the Division of Research Grants and Associate Director of NIH, spoke at the American Rocket Society's "Conference on Anatomy of Manned-Space Operations," in Dayton, Ohio.

The 3-day Conference was sponsored by the American Rocket Society Human Factors and Bio-Astronautics Committee in cooperation with the Aerospace Medical Laboratory and Office of Surgeon, Air Materiel Command, Wright-Patterson Air Force Base, and the ARS Dayton Section.

Dr. Allen's talk was part of a panel discussion on "Government Contracts, Grant and Research Interest in the Biosciences Area." Also participating on this panel were representatives of the Army, Air Force, Navy, Department of Defense, NASA, and AEC.

Dr. Allen discussed those programs of the NIH that can provide support of research activities in space medicine and other related fields. He cited examples of currently NIH-supported projects in these fields which were of special interest to this audience.

Other sessions of the Conference dealt with "Anthropometrics," "Bioinstrumentation," "Bionics," and "Human Factors in the Conquest of Space."

HEW represented on Federal Radiation Council

Dr. Clinton C. Powell, Assistant DRG Grants Branch Chief for Clinical Research, was appointed by the PHS Surgeon General, Leroy Burney, to serve on the Working Committee of the interagency Federal Radiation Council.

Dr. Powell, a Public Health Service expert in the field of radiation, is the representative of the Department of Health, Education, and Welfare on the Working Committee of the Council. Established by Executive order last August, the Council began work on January 4 to formulate policies and make plans for investigation into the field of radiation damage, exposure, and health hazards.

Before taking his present post in March 1959, Dr. Powell was executive secretary of the Radiation and Surgery Study Sections. He came to DRG in 1958 from the Division of Special Health Services, where he was Chief of the Radiological Health Medical Program.

Dr. Powell is a commissioned officer in the Public Health Service. Posts he has held at NIH include: Grants analyst, Research Grants and Fellowship Branch, NCI; staff physician, Radiation Therapy Branch, Clinical Center; and radiation safety officer.

Dr Lindsay speaks at Florida conference

Dr. Dale Lindsay, Assistant DRG Chief, participated in a "Conference on Disease in Early Life," in Miami Beach, Fla.

Dr. Lindsay was the Government's spokesman in a symposium, "Crossroads of Research," a discussion of the integration of support of medical research by Government, industry, and private endowment. Dr. Lindsay outlined Federal support of biological and medical sciences by research grants, training of scientific manpower, and assistance in the construction of health research facilities. He also cited examples of Government-industry cooperation and of liaison between the Government and voluntary organizations.

Other panel members were Truman G. Blocker, University of Texas Medical Branch, Galveston, Tex.; H. F. Zoller, Ethicon Co., Somerville, N.J.; and J. M. Weir, Rockefeller Foundation, New York. Chairman of this session was Hon. Claude Pepper, former U.S. Senator.

This conference was sponsored by the Variety Children's Research Foundation in honor of the January 10 dedication of the Variety Children's Research Foundation Laboratories in Miami. An NIH grant, awarded on a matching fund basis, made possible the construction of this building. NIH officials attending the dedication were Dr. Justin Andrews, Director of National Institute of Allergy and Infectious Diseases; Dr. Robert J. Huebner, Chief of Laboratory of Infectious Diseases; Dr. W. Ray Bryan, Head of Virus Oncology Section, National Cancer Institute; and Dr. Lindsay. Dr. Huebner and Dr. Bryan also took part in the 2-day conference.

HIGHLIGHTS OF PROGRESS IN SUPPORT OF RESEARCH AT NIH, 1960

ITEMS OF INTEREST CONCERNING MAJOR RESEARCH STUDIES AND NEW PROGRAM DEVELOPMENTS IN THE DIVISION OF RESEARCH SERVICES

A variety of technical, scientific, and engineering services are supplied to scientific personnel at NIH and the Institutes as a whole through the Division of Research Services. The 850 employees who perform these services represent a high degree of skill and creative talent plus a wide range of professional and subprofessional specialties.

The Division operates an animal hospital, animal receiving center, and animal farm; it breeds conventional laboratory animals and produces inbred and exotic strains for use in special research projects. The Division has pioneered efforts at NIH to produce germ-free animals on a large scale and offers technologic, advisory, and maintenance services to NIH investigators who are using these animals in their studies.

The Division also serves NIH investigators by supplying the bacteriological and tissue culture media they use, by washing and sterilizing test tubes, pipettes, and other laboratory glassware, and by producing specialized glassware that it not available commercially.

Electronic data processing for the scientific and administrative programs at NIH is available centrally in the Division. Instrument engineering and the design and modification of equipment for special-purpose application in medical research are also part of its many-sided service program. The design of exhibits for display at national and international scientific meetings, all phases of medical illustrating and photographic services, scientific translation and ininterpreting, and the administration of a unique medical library are other research services. A major program is continuous planning by architects and engineers for the location and construction of new research buildings and the remodeling of existing laboratories for new uses.

Frequently, individuals or teams of scientists and technicians in the Division collaborate with Institute investigators on research projects underway, particularly in the service aspects of that research. The Division maintains the high quality of its many services by anticipating the need for and initiating studies relating specifically to the services requested. The cooperative or individual research thus undertaken has a direct application to the research programs of NIH and often results in publication in technical and professional journals or in the form of guides, texts, and manuals. The findings of these studies are thus shared with the scientific public, with other institutions, and with industry.

Fresh egg yolks yield reliable test for isolating "staph" organisms

Among new DRS achievements in environmental sanitation is a simple egg yolk test that has proved to be a sensitive and dependable method for detecting the ubiquitous, and highly adaptable staphylococcus organism. Dr. Lloyd G.

Herman, of the Sanitary Engineering Branch, reported successful use of the test to the Society of American Bacteriologists last spring.

A modified commercial medium, in which fresh egg yolks are the essential added ingredient, is used for the primary isolation of *Staphylococcus aureus* organisms found in clinical specimens and in surgical and patient care areas. The presence of virulent "staph" is readily observed in the strong pigmentation of the colonies, ranging from light yellow to vivid orange, with marked "halos" in the medium.

Because egg yolks are usually sterile, the production of the egg yolk medium is less troublesome than many other enriched media. The modified medium also permits the direct identification of coagulase-positive staphylococci found on routine swabs taken from floors, instruments, sinks, and other sources that tend to be heavily contaminated with other types of bacteria. The high salt content of this medium tends to slow down the rapid growth of the gram-negative species but permits normal growth of the staphylococci.

Military techniques applied to study of biological systems

At a recent symposium, Dr. Norman Z. Shapiro, Chief, Computation and Data Processing Branch, and Richard J. Podolsky, Naval Medical Research Institute, reported on a collaborative effort in connection with computer models simulating models simulating biological activity. Two models of muscular contraction are under investigation, the "sliding" and "folding" hypotheses. Digital computer programs have been written which implement both of these models. Computations employing these programs are then used to verify the agreement of each of the two models with experimental observations, thus obtaining indications of the veracity of the models. The techniques employed are believed to be applicable to a large variety of models of biological systems. They stem from variations of techniques used to implement models of military activities in which a large number of defensive and offensive military elements interact with one another.

NIH acquires rural acreage for development as animal farm

Late in 1959, NIH negotiated an option to purchase 513 acres of farmland in western Maryland about 25 miles from Bethesda. Title to the large tract, known locally as the "Cider and Ginger Farm," was acquired in April 1960. The acreage replaces a small temporary farm where large animals, such as goats, sheep, horses, and cows, have been held for research studies by Institute investigators.

Planning for future occupancy of the farm and its development as a unified research facility began immediately after purchase. A master site plan developed during the year was approved by the Research Facilities Planning Committee. The plan was prepared by the Research Facilities Planning Branch with the assistance of a special consultant employed by the Division of Research Services. Essentially, the plan is a set of guiding principles based on Institute needs and preliminary surveys of engineering problems that could affect the siting of buildings.

Animal waste disposal studies aid design of farm facilities

As an aid to designing sewage treatment facilities for the NIH animal farm, the Sanitary Engineering Branch has completed animal waste disposal surveys at NIH to measure the quality and quantity of waste water discharged during the washing and rinsing of animal cages and kennels, the concentration of detergent in parts per million, and the composition of wet and dry waste production from large and small animals. In related studies at the farm, baseline information has been obtained evaluating the extent of present pollution in the stream passing through the farm to calculate its future capacity for receiving treated liquid wastes.

Variable projection apparatus magnifies 95X on flat surface

Two models of a unique device for "mapping" areas of the human brain have been developed for the National Institute of Neurological Diseases and Blindness by the Instrument Engineering and Development Branch.

The device is a variable projection system for human neuroanatomical reconstruction in research on brain degeneration. It magnifies up to 95 times and projects slide mounted microscopic sections of cortical tissue onto a flat horizontal surface, such as a desk or table top. Heat damage does not occur to the tissue specimens. Distortion of the projected image is avoided by means of double-reflecting mirrors, optical lenses of varying focal lengths, and a modification of a commercially designed projector.

The design, construction, use, and magnification (5X to 40X) of the prototype apparatus have been described in the Anatomical Record. The substitution of more powerful lenses and the addition of an effective cooling system extended the magnification of the second model to the range of 4X to 94X.

No major modification is required to use the system in other research areas or for medical illustrations, training demonstrations, and allied educational purposes. The projected image provides sufficient illumination so that a completely darkened room is unnecessary.

Ingenious drinking fountain installed in animal hospital

An innovation in the animal world is the automatic drinking fountain designed for cats and dogs in the animal hospital by Dr. William I. Gay and John Carter, and reported in the "Journal of the American Veterinary Medical Association." The fountain is a stainless steel basin swinging from a metal bracket attached to a water pipe in an indoor run. A constant supply of fresh water is available through a modified commercial valve assembly. As the water level in the basin drops, a spring opens the valve, and the basin fills with water. A metal cap above the bracket protects the valve from licking or soiling. The fountain is standard equipment in the animal hospital, where it has proved to be economical and efficient.

Photocopier in library increases usefulness to scientific public

With the set of a dial and the push of a button, a scientist may acquire his personal copy of the journal article he has just read before the journal is released for shelf circulation. An automatic photocopier has been installed in the NIH library to print photo-exact copies of textual materials on a self-service basis. Originals may be of any color and any thickness, a feature permitting the copying of any page of a bound book. The new service holds promise for increasing the usefulness of the library's collections of biomedical texts and journals.

New research facilities at NIH have unusual design features

Nineteen hundred and sixty was a peak year in the accelerated building program begun in 1958 to expand and consolidate research facilities at NIH.

Laboratories completed for the Division of Biologics Standards and nearing completion for the National Institute of Dental Research represent an advance in research facility design.

The DBS building incorporates in its design special animal facilities, including a monkey-testing area on the top floor. The NIDR building has a laboratory for germfree animal research. High-pressure air-conditioning systems in each building have filtering devices to trap airborne bacteria. Both buildings have permanent cold and constant temperature rooms, sterile rooms equipped with incinerated air exhaust systems, and movable metal partitions between offices and laboratories so that space can be increased, diminished, or exchanged as needed. Movable partitions have been a custom feature in NIH buildings since the construction of the clinical center.

Also approaching completion was the surgical wing to the clinical center. The new addition will serve as a guide for the design of surgical research facilities throughout the world. A circular structure, with circular operating rooms and wedge-shaped auxiliary rooms, the wing is devoted to cardiac surgery and neurosurgery.

The cardiac surgeries have glassed-in observation domes equipped with television and motion picture cameras. All of the surgeries will be equipped with surgical consoles. These are mobile, stainless steel units connecting the operating tables with central utilities and piped-in supplies of compressed air, oxygen, nitrous oxide, carbon dioxide, helium, and nitrogen.

The air-conditioning system forces air downward from above the operating table to a floor vent underneath. The flooring is a special, nonconductive latex. Hypothermia and blood bank facilities are included in the structure.

Allied construction activity includes a general office building and the new home for the National Library of Medicine, to be located on NIH grounds.

Portable air sampler used in NIH environmental studies

The Instrumentation, Engineering, and Development Branch and members of the Sanitary Engineering Branch have modified a portable air sampler originally developed at Fort Detrick, Md., for use in air pollution studies conducted by the

Sanitary Engineering Branch. The sampler is a versatile apparatus for determining the bacterial content of air anywhere on the NIH reservation. It allows continuous air sampling for either 2- or 8-hour runs at a controlled rate of 15–30 liters a minute. The bacteria are deposited onto a 20-inch long agar-filled tray driven by a motor past a stationary slit. After the tray run is completed, the tray is removed for incubation and later observation of bacterial growth.

The portable sampler is highly adaptable and may use the existing vacuum service in a building or its own mechanical pump. It may be connected to an existing standard 115-volt alternating current line, or, if such electrical service is not available, it can operate from its own 12-volt storage battery. This battery is capable of running both the vacuum pump and the tray driver motor for an 8-hour period.

GENETIC TESTING IS ROUTINE TECHNIQUE IN INBRED MOUSE BREEDING COLONY

Last year the Laboratory Aids Branch announced a rapid skin-grafting technique to determine the genetic purity of inbred mice, and in October it began using the technique for routine testing of mice in the expansion breeding colony for inbred strains. The expansion colony is intermediate between foundation and production colonies of inbred strains. Any difference in genes resulting from errors in mating or from mutations within the strain can be quickly detected with the skin-grafting technique. Tail skin from a female in each new litter is grafted onto the tail of an ex-breeder of the same pedigreed strain. If the graft takes, it can be assured that all siblings will possess the desired genetic characteristics as the breeding stock and that genetic contamination has not taken place. Potentially, skin-grafting can be used as a routine check to determine the genetic homogeneity of all inbred mice issued to NIH investigators.

This technique is described by Dr. Donald W. Bailey and Bashiruddin Usama in "A Rapid Method of Grafting Skin on Tails of Mice," Transplantation Bulletin.

Dictating equipment records oral scientific translations

The use of modern dictating and transcribing equipment has been extended to the recording of scientific translations. Previously it was customary for a translation of a scientific paper to be drafted, edited, and reproduced in multiple copies by the translating service of the NIH library. Now, a translator can bypass the production of written translations by orally translating sufficient information for a scientist to assess research progress in a foreign country that may relate to NIH investigations. The recorded translation becomes his permanent property, to use at his convenience.

Air-conditioned animal transport reduces health hazards

An animal van used to transport the dogs and cats donated by humane societies to the animal hospital was air conditioned last summer to prevent extremely high temperatures within the vehicle. Air-conditioned transport has kept the animals free of the usual discomforts and health hazards associated with excessive heat and close quarters.

Cost disadvantage of disposable test tubes offset by contamination factor

In response to numerous requests, the Laboratory Aids Branch issues one-use clear glass tubes to investigators who prefer a disposable tube for certain flocculation and complement fixation tests. The cost of the new tube is about half the standard multiuse tube, but the high cost of use is offset by the absolute certainty that no organic matter is in the tube, and the assurance that any previous use of the tube can in no way affect current experimental results. Another advantage is the saving of the time and trouble in having to pick over a mass of multiuse standard tubes to select only those clear enough for the tests mentioned.

Low-cost plastic splints may replace plaster of paris

From time to time, the Medical Arts Section collaborates in certain phases of Institute research programs, and as with all research efforts, trial-and-error attempts are frequently necessary before an entirely satisfactory solution is found.

As an example, the section is working with the Rehabilitation Department of the clinical center in its search for corrective or supportive splints that promise a longer life than that afforded by plaster of paris. More than 200 plaster casts or splints are applied to patients annually at NIH. Even though plaster has proved to be extremely effective, there is need for durable splints that cosmetically are more acceptable than plaster. The ideal splint would also be low in cost, light in weight, and easily cleanable. Toward this end, the Department is working with a foam plastic that holds great promise.

In the Medical Arts Section, steps have been taken to develop a plastic wrist splint, which, while it may not prove to be the answer, has provided extremely useful developmental experience. A prototype splint has been made of a plastic blend of styrene and rubber. As a prosthetic device, a styrene-rubber splint possesses several obvious advantages over plaster and the heavier plastics. The splint may be easily removed. Flocking on the interior surface makes the splint comfortable to wear. The plastic is both lightweight and opaque and while it is not flexible, neither is it rigid. Its cost is low, and its fabrication as a splint is so simple that anyone could produce it after seeing a demonstration.

New findings from this search for improved splints and casts will aid the rehabilitation of persons suffering from rheumatoid arthritis. Dr. David Fried, Chief of the Rehabilitation Department, initiated the program.

Special environmental chambers designed and constructed

A wide variety of unique environmental chambers required for the NIH research programs have been in the design and construction stage during the past year. Research requirements for these facilities have challenged the technical skills and ingenuity of the Plant Engineering Branch, which provided the designs and supervised or carried out the construction program.

Plant growth chambers.—Growth chambers constructed for the National Institute of Mental Health were designed to determine the optimum conditions under which plantlife achieves a high enzyme and alkaloid yield. Temperature, humidity, air movement, and air contamination are controlled precisely, with a minimum of variation permitted. The illumination is of a very high intensity, nearly 4,000 foot-candles, to simulate the shady side of a house on a bright day. The information sought may have an important bearing on the role of enzymes and alkaloids in the development of nerve tissue.

Low-level radiation counting facilities.—A low-level radiation counting facility, where "counting" devices and other instruments can record the amount of radioactivity within the human body and other objects without influence from the immediate surroundings, was constructed for the National Cancer Institute. The facility is a physically isolated chamber in which background radiation—from the air, construction materials, instruments, and other room objects—is reduced to a minimum. Isolation of the chamber from the rest of the building is achieved by complete recirculation of the air; airborne contamination from recirculating air is further reduced by filtering the air. The walls, floors, and ceilings of the "counting" cubicles are constructed of steel 6 inches thick.

Hydrogenation laboratory.—A hydrogenation laboratory for the joint use of all Institutes was built with safety in mind. Its primary purpose is to provide safe operation for the high-pressure hydrogenation processes used in various research programs. One wall of the building, which is an extension to the isotope laboratory, faces a natural earthen barrier and is constructed of ¼-inch cement-asbestos board that will give way in the event of high pressures building up within the building itself. As further protection, all electronic equipment is subject to remote control.

Soundproof test rooms.—The construction of independent, enclosed rooms in which NIMH can perform basic research tests on animals, particularly monkeys, without interference from external noise or vibration, utilized plywood, sand, isolation pads, and other standard materials to obtain signification reduction (55 decibels) in sound transmission through walls, floors, and ceilings.

Blood serum cold storage rooms.—Serum storage rooms to provide highly dependable and maintenance-free facilities for storing 600,000 vials of human blood serum at a constant temperature of —20° C. were designed for the collaborative cerebral palsy studies of the National Institute of Neurological Diseases and Blindness. To assure uninterrupted frostfree operation for a minimum of 10 years, duplicate refrigeration machines, hot-gas defrost systems, and emergency sources of electrical service and cooling water were installed.

THURSDAY, MARCH 23, 1961.

MENTAL HEALTH ACTIVITIES

WITNESSES

DR. R. H. FELIX, DIRECTOR, NATIONAL INSTITUTE OF MENTAL HEALTH
DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
RICHARD L. SEGGEL, EXECUTIVE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
	PUBLIC HEALTH SERVICE			
11	Personnel compensation:			
	Permanent positions	4,201	5,335	5,605
	Positions other than permanent	686	534	534
	Other personnel compensation	82	81	62
	Total personnel compensation	4,969	5,950	6,201
12	Personnel benefits	257	298	315
21	Travel and transportation of persons	391	415	428
22	Transportation of things	27	39	37
23	Rent, communications, and utilities	118	120	119
24	Printing and reproduction	36	43	43
25	Other services	1,052	1,477	1,751
	Payment to "National Institutes of Health management fund"	3,500	4,152	4,593
26	Supplies and materials	403	448	462
31	Equipment	366	414	432
41	Grants, subsidies, and contributions	56,272	79,168	68,441
	Total, Public Health Service	67,392	92,524	82,822
	ALLOCATION TO ST. ELIZABETHS HOSPITAL			
11	Personnel compensation:			
	Permanent positions	64	81	81
	Other personnel compensation	4	5	5
	Total personnel compensation	68	86	86
12	Personnel benefits	4	4	4
23	Rent, communications, and utilities	5	10	10
26	Supplies and materials	1		
	Total, St. Elizabeths Hospital	78	100	100
	Total obligations	67,470	92,624	82,922

Personnel summary

	1960 actual	1961 estimate	1962 estimate
PUBLIC HEALTH SERVICE			
Total number of permanent positions	635	836	870
Full-time equivalent of other positions	101	73	73
Average number of all employees	707	785	822
Number of employees at end of year	786	919	950
Average GS grade	7.3	7.6	7.6
Average GS salary	$6,063	$6,741	$6,742
ALLOCATION TO ST. ELIZABETHS HOSPITAL			
Total number of permanent positions	15	17	17
Average number of all employees	14	16	16
Number of employees at end of year	14	17	17
Average GS grade	4.1	4.8	4.8
Average GS salary	$4,154	$4,807	$4,807
Average salary of ungraded positions	$5,188	$5,358	$5,358

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
PROGRAM BY ACTIVITIES			
1. Grants:			
(*a*) Research	23,228	31,308	31,695
(*b*) Fellowships	1,996	2,390	2,390
(*c*) Training	26,197	39,470	28,356
(*d*) State control programs	4,911	6,000	6,000
Total grants	56,332	79,168	68,441
2. Direct operations:			
(*a*) Research	7,206	8,355	9,322
(*b*) Review and approval of grants	1,217	1,541	1,566
(*c*) Training activities	101	99	100
(*d*) Professional and technical assistance	2,062	2,743	2,779
(*e*) Administration	491	649	714
Total direct operations	11,076	13,387	14,481
Total program costs	67,409	92,555	82,922
3. Relation of costs to obligations: Obligations incurred for costs of other years, net	61	70	
Total obligations	67,470	92,624	82,922
FINANCING			
Comparative transfers to other accounts	72	158	
Unobligated balance lapsing	547	2,979	
New obligational authority	68,090	95,761	82,922
New obligational authority:			
Appropriation	68,090	100,900	82,922
Transferred to "Construction of mental health-neurology research facility" (42 U.S.C. 292)		−5,139	
Appropriation (adjusted)	68,090	95,761	82,922

GENERAL STATEMENT

Mr. FOGARTY. The committee will come to order. We have before us this morning "Mental health activities." Do you have a statement, Dr. Felix?

Dr. FELIX. Mr. Chairman, I have a prepared statement which I have filed with the committee. I will not read that unless you desire me to do so. I have a few comments I might make.

Mr. FOGARTY. We shall file your statement.

(Statement follows:)

STATEMENT BY DIRECTOR, NATIONAL INTITUTE OF MENTAL HEALTH, PUBLIC HEALTH SERVICE

Mr. Chairman and members of the committee, it is again my pleasure and my privilege to appear before you in connection with the budget proposals of the National Institute of Mental Health.

Before reporting to you on our programs for the current year and summarizing our programs and our budget proposals for the forthcoming year, I would like, if I may, to present a brief review of the past decade in terms of Institute growth and development.

1960 completed a decade marked by growth and expansion of mental-health activities. During this decade, we have seen a basic transition in the character of the national mental-health effort. In terms of substance and scope, mental-health activities have been broadened to encompass a complex family of diverse disciplines—the biological sciences, the clinical sciences, the social and behavioral sciences, and more recently the physical sciences. We have seen a marked intensification of mental-health activities through the emergence of improved technology, through large-scale cooperative and collaborative research efforts, through expanded community mental health efforts at the State and local level, and through the identification and acceleration of program efforts along specific disease and problem-oriented lines (alcoholism, mental retardation, etc.).

Finally, in terms of accomplishment, the past decade has seen unparalleled advances in terms of contributions to the mental-health field—advances that we can reflect on as a source of pride. Specifically:

(1) We have seen gradual but steady accomplishments in the treatment and control of mental illness. Though mental patients still continue to occupy nearly half of all the hospital beds in the Nation, resident mental hospital populations have continued to decline, year after year. In 1955, with a resident population of 560,576, this new trend was not anticipated. In fact, based on mental hospital data for the period 1944–55, it was estimated that the resident population for 1960 would be 622,170. The 535,332 patients who actually were resident in the 281 public mental hospitals at the end of fiscal year 1960 represented a decrease of 16.2 percent under the projected figure. This overall decrease, moreover, has taken place at the same time that total admissions to mental hospitals have been increasing. The turnover in mental hospitals has been much greater, with more patients being treated more successfully and being released more rapidly.

(2) We have seen the development of tranquilizers and other psychopharmacologic agents which are playing a major role in helping to maintain patients in the community. Followup studies have shown that, in some cases, even chronic schizophrenic patients can make a good adjustment in a normal community environment, given sufficient aftercare and outpatient medical supervision.

(3) We have seen many improvements in the mental hospitals themselves, improvements that have increased their therapeutic potential. New administrative practices, new types of ward management, more highly trained staff, and the increased emphasis on treatment rather than custody which characterizes the new "open" type of mental hospital have brought rich dividends in patient improvement and large numbers of discharges, often after shorter periods of hospitalization.

(4) We have seen a great increase, also, in the number and kind of community facilities available to help the discharged patient complete his convalescence successfully. These include halfway houses, sheltered workshops, ex-patient clubs, followup medical care, vocational rehabilitation, and social services to help the former patient and his family make a successful adjustment.

(5) We have seen an increase in the numbers of people with emotional disorders and mental illnesses being treated in the community without having to be hospitalized in a mental hospital at all. Many more such individuals than ever before are being treated by general practitioners and by psychiatrists in private practice. The number of psychiatric beds in general hospitals has increased more than 35 percent since 1954. Today, there are more psychiatric first admissions to community hospitals than to public mental hospitals. Also, outpatient clinic facilities have expanded considerably. The number of such clinics increased 16 percent between 1955 and 1959, from 1,234 to 1,429, with

every State represented in the latest total. The number of professional man-hours of clinic service available per week for each 100,000 population rose from 115 to 145 during the same period. Most of the patients seen in these clinics can be treated without requiring hospitalization. A survey of a sample of 36,000 patients seen in 185 clinics in 18 different States during 1957 showed that only 8 percent were referred to inpatient facilities. Only 4 percent of the children and 9 percent of the adults who actually received treatment in the clinics were referred for residential treatment.

These hopeful new developments have, in significant part, been made possible or stimulated by the broad-gaged, Federal, mental-health program which the Congress has so generously supported and so wisely counseled and directed during the past several years.

During this past decade of sustained program growth and development, the institute has evolved a program structure that embraces substantially all aspects of mental-health activity—from basic and clinical research and training to the application of research knowledge through disease control, demonstration, and other community mental-health programs. I should now like to report briefly on the status of these broad programs in terms of events of the past decade, current year, and in terms of the forthcoming year with particular emphasis on those program developments that are showing special promise together with some of the patterns of progress that appear to be emerging in terms of the decade ahead. For convenience, I would like to present these developments in terms of our three broad areas of program effort: (1) our extramural research, training, and community service programs; (2) our intramural research programs; and (3) our program development activities which have proven so effective in the planning and implementation of new and developing areas of program emphasis and need.

EXTRAMURAL PROGRAMS

Training program

Over the past 12 years, the basic role of the Institute's training program has been to support the production of professional manpower in order to implement a comprehensive mental-health program. The manpower needs in the mental-health field, as in all other professional areas, have intensified even more rapidly than the field has been able to produce qualified personnel. In fact, the vigorous growth and development of the mental-health movement in the past decade has contributed to its own manpower shortage by increasing the public awareness of the importance of mental health and by heightening the demand for treatment and research against mental illness.

The primary aim of the program has been to increase as rapidly as possible the number of specialists and to improve the quality of training in the mental-health professions. This objective has been pursued with consistent efforts to broaden the scope of what can appropriately be considered relevant to mental health. The priorities as to where training support should be concentrated have been modified as the total program has grown and as new needs in the field have become apparent. At first, support was confined to training programs for specialists in the four, generally recognized, mental-health disciplines plus a modest program for training of research personnel. Subsequently, this basic support for graduate training in psychiatry, clinical psychology, psychiatric nursing, and psychiatric social work was augmented by support for such areas as: (1) undergraduate grants in psychiatry and psychiatric nursing to improve psychiatric teaching programs; (2) grants to schools of public health for the improvement of the mental-health content of the curriculum; (3) pilot project grants to stimulate the development of new and experimental methods of teaching in the field of mental health; (4) grants for career teachers to encourage persons with exceptional potential to choose careers in teaching and to provide support for them during the training period; (5) grants to provide psychiatric training to general practitioners and other physicians in practice; (6) grants to provide research training of relevance to mental health in the biological and social sciences; (7) grants to foster the integration of the behavioral sciences into the education of the modern physician; and (8) research fellowships.

The above is not a complete list, but is representative of some of the major areas of growth over the past 12 years. By their very existence, these areas are evidence of a series of significant accomplishments within the training program. The assistance by grants of these programs represents, in many instances, new departures for training in mental health.

These areas of grant support are, however, only vehicles for achieving the actual objective of the training program: the increased production of better qualified, mental-health personnel. It is pertinent to note that, from the initiation of this training program in 1947 through 1960, a total of almost 10,000 individuals have received 1 or more years of support for professional training in the mental-health fields. An even greater number of persons have received indirect benefits by participating in the various training programs supported by these funds.

As a result of its vigorous growth, the total operation of the Institute's training program is today a major influence on the mental-health fields. At the present time, practically every medical school department of psychiatry is assisted by a National Institute of Mental Health training grant. Almost all the major graduate departments of psychology, graduate schools of social work, and graduate schools of nursing are also assisted by training grants from this source. In most cases these include traineeships. In addition, other training centers, including many of the major psychiatric training hospitals, child-guidance clinics and private, nonprofit, psychiatric treatment centers as well as clinical psychology internship centers, provide training facilities and traineeships made possible in part by Institute funds. Grants are also provided to over 70 schools of nursing with basic collegiate programs for strengthening the psychiatric teaching of undergraduate nursing students.

Turning to the more immediate past, the last year has seen program consolidation and a series of administrative changes in training program operation. An important administrative advance was made when the Congress made it possible for us to allow for the advance notification of graduate training grant awards. This change in the award cycle was initiated in 1960 and completed in 1961. Final notification of awards in 1962 will thus be made well in advance of the beginning date of the grant in the academic cycle as contrasted with the previous circumstance requiring notification which was often 3 to 4 months subsequent to the proposed beginning date. This latter situation, over the past few years, imposed severe hardships on the grantees.

Some of the highlights of program operations within the last year are to be found in areas of support which were initiated within recent years. Support for training in the biological and social sciences, which had begun in 1957 on a pilot basis, was further implemented in 1960 through a formal announcement to appropriate training centers of the availability of grant support. Grants in these two areas are mainly for interdisciplinary training of biological and social scientists who can thus bring a new approach to bear on problems of mental illness. Funds are also available to provide research training in these basic sciences to persons earlier trained in mental health. As the nucleus of scientists with this kind of training completes its graduate training and develops new research projects or joins older colleagues in existing research programs, the scope of this kind of interdisciplinary research will increase. It is already clear, from noting the background of some of the more productive and gifted research workers in the mental-health field, that a combination of training in a basic biological or social science plus some clinical experience with mental illness provides the recipient of such training with an excellent perspective for fruitful examination of research problems in mental illness. It seems almost axiomatic that in an area of research endeavor as complex as mental illness the multidisciplinary approach should have the greatest yield.

The emphasis on this kind of interdisciplinary approach will continue and will increase in 1961 over the 1960 level. As the training centers in the biological and social sciences continue to explore training with a mental health orientation, an increasing number of meritorious applications can be expected. These will not only be interdisciplinary in nature, but will include such critical areas as psychopharmacology, biochemistry, physiology, epidemiology, and sociology. A high proportion of the grants in the biological sciences include considerable emphasis on psychopharmacology. There is a critical shortage of qualified personnel in this area and vigorous efforts are continuing to expand the base of training support already established.

Support for the psychiatric training of general practitioners is another area which has been marked for high priority development. The program has expanded almost threefold from its 1959 level of support at $1,300,000 to a 1961 level of support at $3,800,000. In each year the entire amount has been awarded. An analysis of the awards made in the first 2 years, 1959–60, reveals that approximately 200 physicians received support for psychiatric residency training, half of whom are already on a second year of award. About two-thirds of these physicians were previously in general practice, about 15 percent formerly specialized in pediatrics and about 10 percent came from internal medicine. These physicians, almost half of whom have had 10 or more years of professional experience in their respective specialties, represent a significant increase to the pool of psychiatrists in training. Furthermore, they bring with them a wealth of valuable medical experience to enrich their psychiatric training and to increase their capacity to use the psychiatric skills they learn.

Another important recent program development is the initiation in 1960 of support for training programs in medical schools which will lead to the integration of the behavioral sciences with the education of the modern physician. This type of training is providing a broader scientific base for understanding human behavior, and the faculty in these training centers will provide the model and the stimulus for an increasing proportion of medical students to consider research careers in the behavioral sciences. This program began modestly in 1960 and is being expanded in 1961. The potential for growth of this area of training is considerable, and continued efforts will be made to support this growth.

The Institute for a number of years has recognized the severe national shortage of qualified research investigators and has expanded its support for research training through its various fellowship programs. The increase in applications for fellowship support during 1960 and 1961 has indicated that careers in mental health research are steadily becoming more attractive. Research training programs in graduate schools are multiplying, with a differentiation and a sharpening of focus in many fields of research.

Since the purpose of the Institute's fellowship program is to train scientists for research in the whole field of mental health, and since the potential of this research demands a much larger number of qualified scientists than is now available, the Institute has actively encouraged the growth of this program, as training facilities permitted. In 1959, for example, the number of applications was 438 and the number of awards 287; in 1960, 764 applications were submitted and 484 awards made, and in the current year based on the experience of the first half of the year approximately 1,000 applications will have been submitted and 760 awards made. New types of special fellowships, senior fellowships and career research professor grant programs were also established during 1961, and the continuation and extension of these programs in 1962 is an important necessity of the overall research training program.

In describing these highlights for this year it is important to reemphasize the role of our training program as a vehicle for implementing new methods of professional education as well as expansion and improvement of traditional approaches. The vigor of the field makes it receptive to change. This change has been quickened as a result of various symposia and conferences held under the auspices of the national professional associations and financed by special grants from the training program. In all four of the major professional fields concerned with mental health—psychiatry, psychology, social work, and nursing—important developments in professional education have resulted from conferences financed by training grant funds. In recent years these have included a major conference on graduate education in psychology held in 1958, a major conference on research training in psychiatry held in 1959, a national conference on curriculum planning in social work held in 1960, and a national conference on the education of the clinical specialist in psychiatric nursing which was held in 1956.

As with the rest of the Institute program, but perhaps to a greater extent, the future of the training program needs to be viewed on a long-range basis. The shortage of professional personnel will not go away. In this context it is appropriate to mention that we are actively engaged in efforts to improve the status of manpower information in the mental health field so that eventually better data on supply, utilization, and demand will be available for program planning. Developments along these lines will be reported at the earliest possible time.

The training program in its present operation is a comprehensive effort to meet the increasing need for mental health manpower. As a major resource for stimulating the production of such manpower, it is important that this program continues to grow as the total national effort to improve mental health continues to grow.

Research grant program

The research grant program is a major instrumentality in the overall planning of the Institute. Through the persistent efforts of hundreds of grant-supported research investigators throughout the country, we have steadily moved forward in our knowledge of the etiology and treatment of mental disorders. A long and difficult road is still before us.

Over the 13 years in which the grant program has been in effect there have taken place far-reaching changes both in the size of the operation as well as in the nature of the research being supported. The number of grants supported in 1960 alone, for example, was 14 percent larger than the total number of projects completed in the preceding 11 years between 1948 and 1959. The $6,372, for example, which in 1948 represented our total grant expenditures in problems of aging, has swelled to an estimated $1,204,000 by 1961. The now vital program in psychopharmacology, today over one-fourth of the total research grant program, was nonexistent in 1948. Development of new research techniques, also, has resulted in a pronounced increase in the numbers of studies of the biological and physiological aspects of mental illness. New biochemical and neurophysiological tools, broadening the base of disciplines engaged in mental health research, have brought a larger community of scientists with a greater variety of approaches to the field. Today we see a program whose scope crosses through psychiatry, psychology, sociology, anthropology, and other social sciences, in addition to such biological sciences as neuroanatomy, neurophysiology, biochemistry, neurochemistry and genetics.

We have also seen a progressively greater research emphasis on the early formative years of life—on research in child development and the early prevention of mental illness. The integration of understandings from psychiatry with understandings from psychology and sociology has also broadened the scope of current research.

In recent years we have seen within the research grant program the development of new and more varied types of grant support designed to meet more effectively the needs of the field and of research investigators working in it. Outstanding scientists of proven productivity may now hope for long-term, stable "programatic" support of their research, providing a freedom and flexibility hitherto very difficult for their studies.

From the start of the research grant program, the Institute has believed strongly in the support of basic and methodological research. Support for these studies continues to command a proportionately heavy share of the grant program today, with a long-term goal of better understanding the basic biological and psychological functions and dysfunctions of man, of normal and abnormal growth and development.

The improvement of the care and treatment facilities in mental hospitals has been a primary goal of the Institute's program over the years and is also actively being fostered through the research grant program. Although new emphasis is being placed today upon outpatient care and community facilities, important research is being continued upon the social environment of the mental hospital as it relates to the patient's recovery or relapse. During 1961 the Institute's grant program is supporting a variety of research studies leading toward an understanding of social interaction in the hospital, studies of the institutional structure of public mental hospitals as they reciprocally influence and are influenced by treatment programs, studies of patients' social adaptation to mental hospitals and research analyzing the role of patient-staff relationships.

Over one-third of the total research grant program in 1961 is related to research on schizophrenia, a major medical and social problem in the United States. More than half the patients hospitalized for all mental disorders are diagnosed as schizophrenic; they occupy one-fourth of all hospital beds in this country.

Pharmacologic agents and hospital care are, of course, important adjuncts in the treatment of schizophrenic patients. Recent research also continues to indicate the value of intensive psychotherapy not only as a treatment method but as an avenue in understanding the schizophrenic process as a whole.

Research on the effectiveness of the various convulsive therapies in the treatment of schizophrenia is also underway. The discovery that certain drugs will produce convulsive seizures equivalent to electroconvulsive therapy has also led to comparative testing of the effectiveness of agents like Indoklon as opposed to electroconvulsive therapy (ECT). Ine one study at a Maryland State hospital, Institute supported investigators have found hexafluorodiethyl ether a safe alternate treatment procedure to ECT.

The Institute plans to continue to invest a heavy share of the research grant program in research related to schizophrenia, not only with respect to its treatment, but in study of the multiple etiology of this severe mental syndrome. Support will be extended for research not only into the biological and biochemical aspects of schizophrenia, but into what may be termed psychogenic theories of schizophrenia. An increasing number of these latter studies deal with the family interaction of schizophrenic patients. Further research is particularly needed into problems of diagnosis and improved diagnosis in childhood mental disorder.

The Psychopharmacology Service Center was established in late 1956 by the National Institute of Mental Health to develop a national program of research dealing with the clinical efficacy and basic mechanisms of action of the newer psychiatric drugs. The success in stimulating a broad and expanding program of both basic and clinical research in this area is readily evident. Investigators (university, pharmaceutical industry, etc.) have developed many new drugs during this period of time. Most of the drugs now available for general prescription use are under study in a number of individual clinical investigations.

Many of the new psychiatric drugs have continued to demonstrate their general clinical usefulness and are in part responsible for the gradual decrease in the number of resident patients in our public mental hospitals. Moreover, a series of grant-supported studies has recently underlined the effectiveness of certain of these drugs in maintaining chronic psychiatric patients in the community at reasonable levels of social adjustment.

The Institute, through the staff of the Psychopharmacology Service Center and with the advice and guidance of its advisory committees, is constantly evaluating work now going on in this field in order to identify areas in which special staff activity is indicated.

As a result of such staff-committee interaction during the past year, the Institute has developed several programs designed to meet the evident needs of the field.

A new program for the support of early clinical drug evaluation units has been developed and formally announced. Twenty-two proposals requesting support for the establishment of such units have already been received and are currently being reviewed. It is anticipated that by the late spring a group of from 5 to 10 such units will be under support and actively engaged in the evaluation of new psychiatric drugs.

The pharmaceutical industry, utilizing a variety of animal screening procedures, has been very actively engaged in developing promising new chemical substances with possible utility in the treatment of psychiatric illnesses. Unfortunately, the results obtained from animal screening procedures cannot be used fully in predicting which compounds will be effective in the treatment of specific psychiatric conditions in man. More intensive work is therefore needed at the early clinical screening level to insure that promising compounds are adequately studied for preliminary indications of efficacy, and that detailed evidence concerning their clinical properties is available at such time as they may be made available for general clinical use by practicing physicians. Work of this sort has suffered from lack of stable long-term support. This new program will greatly increase the Institute's contribution to this phase of drug development and will provide needed support for specialized units engaged in this activity.

Grant-supported research continues to provide interesting information concerning drugs now already in clinical use. Chlorpromazine, the first phenothiazine derivative identified as having antipsychotic properties, continues to be reported to be the most effective drug. The newer phenothiazine derivatives which are also being used in the treatment of schizophrenic states have not yet been shown to be significantly superior to chlorpromazine in effectiveness, although two grant-supported studies—one at Spring Grove State Hospital in Maryland, and one at Napa State Hospital in California—have reported that triflupromazine is at least as effective as chlorpromazine and may cause fewer undesirable side effects.

Two of the most interesting new phenothiazine derivatives are fluphenazine which is reported to be about as effective as chlorpromazine at one one-hundredth the dose but produces a higher incidence of neurological side effects, and thioridazine which is reported effective at a dosage range comparable to that of chlorpromazine but almost completely lacks neurological side effects. These 2 drugs are the most interesting of the group of 11 phenothiazine derivatives now available for general prescription use. They have not yet been compared with chlorpromazine in controlled clinical studies. For this reason a nine-hospital collaborative study has been planned and developed by the Institute which will compare these three drugs in the treatment of acute schizophrenic patients. Since the hospitals participating in this study will range from well staffed private psychiatric hospitals to relatively less well staffed State mental hospitals the results obtained from this study will have broader implications than any single project at one hospital could achieve. In addition, the data collected in this collaborative study will throw light on the effects of different hospital milieus upon the response of schizophrenic patients to drug treatments. It has often been suggested that drugs work better in public mental hospitals than in well staffed private or university hospitals. This collaborative study will be the first systematic attempt to provide the data necessary to evaluate this hypothesis.

The Institute, through the Psychopharmacology Service Center, is continuing to expand the services available to investigators in the field of psychopharmacology. The Center's scientific information unit now has on file approximately 12,000 documents dealing with research in psychopharmacology including reprints, books, manuscripts, and monographs. These materials are coded in such a way as to be readily utilized for the preparation of special bibliographies and other scientific informational materials needed by investigators in this field. These documents are also most useful to the staff of the Institute in planning special research activities in psychopharmacology. Special provisions have also been made for the translation of articles in foreign languages.

The Psychopharmacology Service Center Bulletin is one of the chief means by which information has been disseminated. The bulletin is now sent to approximately 3,500 investigators in the field of psychopharmacology, of whom approximately 1,500 are located outside the United States. In addition, a special handbook covering all research on the effects of drugs on animal behavior is being completed and should prove most useful both to investigators carrying out research in this area and to investigators interested in developing improved techniques for the screening of new psychiatric drugs.

During the past year the Institute has also established under contract a specialized unit at George Washington University equipped to handle the increasing volume of data deriving from research projects in psychopharmacology supported by the Institute. This unit is also equipped to provide the Institute and investigators referred by the Institute with assistance in the statistical planning of experiments in psychopharmacology and in the devising of the most expeditious methods for the collection and analysis of the data involved.

The contract mechanism is also being utilized to support the synthesis of chemical compounds needed by investigators doing basic research on the mechanisms of drug action which are not available through the usual commercial channels.

The Institute has also affirmed in its research grant program the increased recognition by the American public of the mental health implications of a number of crucial social problems—among them aging, juvenile delinquency, mental retardation, alcoholism, and drug addiction. We have seen in the last decade, a developing sense of public responsibility for better solutions to these problems which affect so many of society's members, and at the same time an increasing demand on State and National agencies to assist in supporting research in these areas.

Among those social problem areas which are of special concern in the research grant program, the subject of aging involves the greatest number of people. This year the White House Conference on Aging has focused some of our national concern with problems of older Americans. The Institute has been interested in supporting not only research oriented toward the alleviation of individual suffering and the social costs associated with the process of aging, but with studies channeled toward the mental health and social well-being of the aging population.

In general terms, the Institute's approach to problems of aging may be described as possessing three broad fronts; research on the pathological processes associated with the aging process; research on the normal and nonpathological aging process; and research on the assets of the aged so that they might be more fully utilized in achieving and maintaining mental health.

From the start of the research grant program in 1948, the Institute has made periodic assessments and evaluations of the program with an aim of anticipating and meeting more effectively the needs of the field. During 1960 a major coding and classification system to permit automatic data processing of detailed infor-fation on its research grant program was established. The results of these and other analyses now enable a close scrutiny of many aspects of the overall grant program, among them the scientific fields of study involved, the disciplines and training of all investigators, the types of institutions in which investigators are working, disorders and symptoms studied, clinical goals of the research, and many other factors. Through examinations utilizing the unique statistical information now available from the grants classification program, through individual staff investigations of special research areas, and through the support of specialized research conferences, the Institute is steadily defining the needs of mental health research. Information of this nature assists the Institute on a continuing basis in guiding the program, as may become necessary, into new areas of research. Concurrently, the information being gathered by Institute staff is being made available to research investigators and interested professional and governmental organizations throughout the country to assist in the development of a sharper national perspective on research needs in mental health.

We have been enabled, through one type of comparative fiscal scrutiny, to recognize the trend toward larger grants. The mean annual award for all the Institute's research grants more than doubled between 1948 and 1960. Whereas in 1954 only 2 percent of its research grants were for amounts over $50,000, in 1960, 10 percent were in this category. The substantial growth in multidisciplinary research since the start of the program is reflected not only in the increasing cost of research, but in changes over the years in the professional fields now engaged today in the mental health research effort.

Community services

Fifteen years ago, few would have predicted the startling progress that has been made in State and local mental health programs. Community mental health programs were few and far between; the mental health program in most places was the mental hospital alone; trained mental health personnel were extremely scarce; the public attitude toward mental illness was pessimistic and repressive. In 1946 only seven States had organized community mental health programs. Today every State has an organized program. The initiation of Federal grants-in-aid to States for community mental health services resulted in State and local funds increasing from $2.6 million in 1949 to $60 million in 1960. There were 1,429 outpatient mental health clinics in the United States in 1959; about 3 times as many as existed in 1946. Every State now has at least one outpatient clinic.

Revolutionary changes are now taking place in State mental hospitals. Voluntary admissions, open hospitals, the concept of the hospital as a therapeutic community and the psychoactive drugs are transforming many of our hospitals. Treatment, not just custody, is the objective. A more optimistic and hopeful attitude about returning patients to the community has resulted and increasingly there has been a real basis for this optimism. The hospital's responsibility for the care and treatment of the mentally ill is being shared more and more by the community—through outpatient clinics, general hospitals, private practitioners, aftercare and rehabilitation services.

In the last few years a remarkable increase has occurred in the number of psychiatric units in general hospitals. A recent survey of psychiatric patients in general hospitals (issued by the Joint Information Service of the American Psychiatric Association and the National Association for Mental Health) revealed that in 1958 the number of psychiatric admissions to general hospitals was larger than the admissions to State mental hospitals. Between 1954 and 1958, the number of general hospitals in the United States accepting psychiatric patients increased by 40 percent—from 563 to 789. Of the general hospitals with over 500 beds, 90 percent reported that they admit psychiatric patients. Psychiatric units still are, however, most common in the large general hospitals in cities.

Only a short time ago, the concept of day-hospital care and night-hospital care was relatively unknown. The recent survey of general hospitals by the Joint Information Service found that there were 76 general hospitals in the United States which had day programs for psychiatric patients that did not remain in the hospital overnight. Fifty-three of the U.S. hospitals had night-care programs for patients. Altogether close to one-tenth of the U.S. hospitals surveyed had either a day- or night-care program.

Marked gains have been made in increasing national rehabilitation services for the mentally ill and mentally retarded. The number of mentally ill persons prepared for and placed in successful employment through the Federal-State program of vocational rehabilitation increased from 1,793 in 1955 to 4,000 in 1960, a rise of 123 percent. The percentage gain for the mentally retarded was even larger—314 percent. The program of community services developed by the Institute has been one of the powerful factors in the progress made by State and local programs in recent years. Three major techniques are used: (1) Professional and technical assistance, (2) grants-in-aid to States and (3) mental health project grants. The coordinated use of these resources to buttress and supplement each other has been a major strength of the program.

The focus of our community services activities is on helping State and local mental health programs and is primarily concerned with the provision of mental health services to the people of the Nation. This, after all, is the major end result which our society expects to derive from the training and research programs. The goal is to develop high-quality, comprehensive, coordinated programs for the promotion of mental health; the prevention of mental disorders and the care, treatment, and rehabilitation of the mentally ill.

The community services program serves as the major channel for mobilizing the resources of State and local mental health programs in achieving national mental health objectives. Through the operations of Institute staff and especially the regional mental health representatives, it is possible for the National Institute of Mental Health to reach out and provide a communication network for the dissemination of knowledge to all States and communities as it becomes available from basic and operational research. In the other direction, the staff serves as eyes and ears of the Institute. From continuous contacts with staff in ongoing State and local programs, feedback is provided on needs, problems, and areas requiring development in the research and training programs. Empirical findings from practice often serve as an essential first step which can be followed by more rigorous testing through formal research. Some of the most fruitful new concepts and methods of patient care and treatment have come from practitioners and administrators who have experimented informally in their day by day work with patients. Those innovations include emergency psychiatric care, the therapeutic community, open hospitals, and day and night hospitals.

Many States are investing funds in research activities and are asking for help and guidance in developing sound projects and methods: these research activities both supplement and complement the work being done by the research program of the National Institute of Mental Health.

Many examples of new and challenging approaches in programing by the States could be given. The following are just a few:

Paralleling the interest in day hospitals for adults. experimentation is underway with day-treatment centers for seriously disturbed children. In Tennessee, a mental health clinic is experimenting with a day-care school for a small number of psychotic children. Federal grants-in-aid funds are being used to support two day-treatment centers for emotionally disturbed children in New York and a day-care program for autistic children at the Bridgeport, Conn., Rehabilitation Center.

The Northeastern South Dakota Mental Health Center (Aberdeen) is placing major emphasis on emergency treatment—very brief, supportive and medical treatment, including the use of drugs. The program is unusual because services are available on call, both personally and by telephone call outside of regular office hours, and efforts are made to visit the patient when the patient is not able to come to the office.

As an example of a general hospital which provides an unusually comprehensive program, the Montefiore Hospital, New York City, opened its psychiatric unit in 1960. The program includes inpatient services, day care, night care, outpatient clinical services, and home care, including visits by resident psychiatrists to the homes of patients or their families.

Kentucky is developing "open door" plan in all four of its State mental hospitals.

In Iowa, at the Clarinda Mental Health Institute, the hospital has been reorganized into units of care based on county geographical boundaries. The patient is admitted directly to a unit which serves the county rather than to a traditional hospital unit such as an acute ward or a chronic ward. The psychiatric team which cared for the patient in the hospital, follows the patient into the community to help him plan for his convalescence, whether in his own home, in a foster home, or a nursing home.

Public health nurses in local health departments in Alabama have primary responsibility for aftercare. Nearly half of the State's 67 counties now have such services. In many Alabama counties the local mental health association is participating in these services by provision of drugs.

Delaware has day-care centers that serve mentally retarded children when they have an IQ below 35—a group usually considered to require institutional care.

Rhode Island, in collaboration with the National Institute of Mental Health, has inaugurated an information referral and consultation service for the mentally retarded. The major purposes of the demonstration are identification of the range of needs, the resources necessary to meet these needs, effective ways to bring the retarded into relation with the mainstream of community services, and to obtain data that would be useful to other communities planning services for the mentally retarded.

An outstanding mental health service for the aged is Senior Citizens, Inc., a community center for elderly people in Nashville, Tenn., which combines a program of services, training and research. An increasing number of the aged served by this center are homebound and they are being provided with medical care, social services, and instruction in self-maintenance.

A study sponsored by the California Department of Public Health and the American Medical Association at Mount Zion Hospital in San Francisco, revealed that acute alcoholics can be successfully treated in a general hospital without segregation, without restraint, with no more trouble than other acutely ill patients. During this project 62 patients were admitted, a few at a time, for periods up to a week or more. They were treated only for the worst part of their acute alcoholism episode. For help with their deep-seated emotional problems, they were referred after discharge to psychiatrists, an alcoholism clinic or Alcoholics Anonymous.

In 1955, the technical assistance project, a highly successful, administrative device, was developed by the Institute. In these projects, outstanding national experts meet with State staff in an institute or workshop focused on a specific mental health problem. Since 1957, 88 such projects in 36 different States were completed, covering a wide range of subjects, including aging, alcoholism, delinquency, and educational workshops for clergy and lay groups. Results are published and disseminated widely.

Another innovation which has had great impact on the field is the mental health project grants program begun in 1957 as a result of the passage of title V of Public Law 84–911. The mental health project grants are awarded primarily for the development of new and improved methods in the care, treatment, and rehabilitation of the mentally ill including improved methods of operation and administration of institutions. The program was developed to better meet the needs of the mentally ill by stimulating experimentation, demonstration, and research within mental hospitals as well as in community programs focused on preventative services and post-hospital care. It pursues its aim not only in the support of studies which hope to add specific scientific knowledge to the field but, also, by supporting projects which will stimulate the growth of interest and skill in mental health programs; encourage isolated systems to participate in progressive mental health activities by utilizing improved methods and techniques; and by supporting projects designed to develop better methods of organization, communication, and utilization of existing services, facilities, and personnel.

The program emphasizes three broad approaches: (1) improved hospital care and treatment; (2) improved administrative practices; and (3) improved community mental health programs. Special consideration is given projects designed for these purposes when they pertain to critical areas such as alcoholism, aging, juvenile delinquency, mental retardation, or schizophrenia.

The range of project support is illustrated by examples such as the study being conducted at the University of Texas Medical School in Galveston. This project is focused on a method of prividing services in rural areas to disturbed adolescents who would ordinarily require long-term and probably institutional care. The adolescent and his family come to the Texas Medical Center for 2 full days. During this time the treatment team concentrates its full time and facilities available in working with the family in terms of effective utilization of family strengths in meeting the crisis. Followup studies of these cases at the end of 6 months and 1 year indicate significant improvement in the majority of families studied and are beginning to yield clues as to the appropriate selection of cases for this method of treatment. Tentative exploration is proceeding in applying this method with other clinical groups and with different age levels. It is possible that this method can be utilized in providing services for people in rural areas where psychiatric facilities are scarce or nonexistent.

Another is a collaborative study of the University of Kansas and the State Hospital and Training Center at Parsons, Kans. The project is designed to develop concepts and procedures to facilitate more adequate language and communication behavior among institutionalized mentally retarded children. The research activities involve the development of a systematic approach to language and communication as an interpersonal process, the refinement of a descriptive system for classifying verbal behavior, the development of language treatment methods for retarded children, and the development of procedures for studying and modifying communication behavior in the environmental setting. The project utilizes an experimental cottage where trained aides employ a variety of language stimulation procedures. Laboratory studies are utilized to sustain both short- and long-term treatment methods. The methods developed in the laboratory are tried and evaluated in the cottage environment and the laboratory, in turn, develops hypotheses derived from observations in the cottage milieu.

Through mental health project grants, support is provided to a wide variety of projects designed to promote knowledge concerning such problems as: Modes of prevention and early detection of mental illness; more effective and more economical alternatives to conventional hospitalization in a mental institution; rehabilitation and reintegration of discharged patients into the productive life of the community; procedures for developing and stimulating community interest and understanding concerning mental health and mental illness; better utilization of existing agencies and services; and increasing participation of personnel in other than the traditional mental health disciplines in the network of services for prevention, treatment, and rehabilitation.

Many of the projects are directed toward exploring and evaluating new treatment methods and techniques such as emergency treatment in the community at time of crisis, immediate service in outpatient facilities, day and night hospitals, halfway houses, psychiatric services in general hospitals, open hospitals, smaller units in mental hospitals based on the therapeutic community concept, and increased participation by general practitioners, nurses, social workers, social scientists, and other skilled personnel in mental health programs.

There has been a regular and substantial increase in the number and quality of requests for support through the program of mental health project grants. Many applications are directed toward the improved coordination and cooperation of existing services and the interaction of patients, staff, and community to provide continuity of care and sufficient flexibility of programs to meet the needs of the individual with appropriate resources. An increasing number of projects represent collaborative efforts of two or more agencies; this is of particular significance when it involves a university and a service program so that each can complement and enrich the needs and skills of the other.

Although there has ben a vast increase in knowledge concerning the mentally ill and new techniques have been developed that show promise of being effective, they have been tried out only in limited situations. There is urgent need to test and demonstrate these techniques in a variety of settings to provide knowledge as to how and where they can be used to maximum advantage in the total program of prevention and treatment. It is essential to know the adaptability of new methods to different age levels, categories of illness, and various cultural groups as well as to measure and evaluate their impact on families, the hospital, and the community. The program of mental health project grants provides a mechanism through which progress can be made toward these objectives.

During the past decade certain principles and guidelines for the development and growth of community services programs have become increasingly evident.

Much of our knowledge about mental health is fragmentary. Final answers to problems are generally not yet available so that the field needs to be open-minded and flexible in developing programs. There is continuing need for experimentation, research, pilot projects and evaluation. Experimentation with new approaches, methods, and techniques should be encouraged.

The gap between present knowledge and present practice should be narrowed. The collection and dissemination of information about mental health programs, the publication of technical articles, individual consultations, and the sponsoring and financing of seminars, institutes and workshops, have proven to be good devices by which the Institute can assist State and local mental health personnel to keep abreast of current knowledge.

As a long-range goal, mental health services should be available for all in the population that need these services since large areas of the country, large segments of our population still have little or no mental health services. Communities should have a coordinated continuum of services, beginning with preventive services and including care for the mentally ill as they move from the prehospital period, through inpatient care and back to the home. Mental hospitals and community programs need to work together closely.

Preventive mental health programs should be expanded. A 1-to-1 therapeutic relationship cannot be available in the foreseeable future to all people who need it. Mental health concepts and philosophy should be incorporated into the practices of the many different community agencies and institutions dealing with people. Mental health education, mental health consultation to health and welfare agencies, courts, schools, general practitioners, volunteer agencies, etc., should be an essential part of the activities of State and local mental health personnel.

Community mental health programs should have a public health emphasis on prevention and control: they should be concerned with the total population and with the community and its organizations and groups. The tools and techniques of public health (i.e. epidemiology, early case-finding, prevention, etc.) seem to offer a fruitful approach for the development of community mental health services.

The development of mental health services is a joint and cooperative responsibility of Federal, State, and local, public and voluntary organizations. Local support tends to assure the continuation and growth of mental health programs.

In the use of grants-in-aid funds to State mental health authorities and in consultation with States, staffs have worked for the establishment of a strong, well-qualified core of professional mental health staff at State level in an integrated governmental unit responsible for mental health. These State level staffs have been considered as essential for leadership in "charting the course" for State and local programs.

The Institute has not considered that it has sole responsibility for training and research. State, local, and voluntary organizations have been stimulated to develop their own educational and research programs. The advantages of an integrated program of training, research, and services have been stressed.

The last 15 years have been a remarkable and exciting period in the history of mental health. The real progress made in almost every part of the Nation should not obscure the vast deficiencies in the Nation's services. No community in the United States has a comprehensive, coordinated mental health program providing a continuum of services. Modern mental health facilities and programs are mostly concentrated in the large, urban States. Far too many rural areas have no mental health service other than the distant, antiquated State hospital. Not enough States and communities have as yet developed mental health services in the social problem areas of aging, alcoholism, juvenile delinquency, mental retardation, etc.

It is an ongoing responsibility of the National Institute of Mental Health to provide information, advice, council and support to the States to aid in the development of comprehensive services for the people.

INTRAMURAL RESEARCH

The past decade has seen striking growth, both in size and complexity, of the intramural research program of the National Institute of Mental Health. Beginning with the opening of the Clinical Center in 1953, we have made steady and satisfying progress in the development of this important segment of our research effort. The Clinical Center has provided us with a splendid facility for our researchers to engage in true multidisciplinary research, for the cross-fertilization of ideas, for the subjection of new laboratory findings to critical analysis by other research disciplines as a basis for more rapid exploitation in terms of clinical application. More recently, the establishment in 1957 of a new facility for research in clinical neuropharmacology in cooperation with Saint Elizabeths Hospital has added another broad dimension to the Institute's research effort for the study and investigation of the action and mode of action of pharmacological and other agents which affect mental functions. Currently, we are proceeding with the planning and construction of more adequate animal research facilities for our Addiction Research Center in Lexington, Ky. And finally, we are enthusiastically planning for the construction of the joint Mental Health-Neurology research building to house our basic science and psychopharmacology research programs at Bethesda.

With gradual growth and development of our physical facilities, we have also made very satisfying progress in the acquisition of our professional research staff. During a period of rapid growth, we have attracted a number of brilliant young scientists together with a cadre of established leaders in their respective fields—elder statesmen if you will—to complement our earlier nucleus research staff. And with respect to research accomplishments, we have made steady progress resulting in part from the quality of our research staff and in part from the special research opportunities afforded by our physical facilities.

I will not dwell extensively on the research accomplishments that have characterized the past decade, but I would like briefly to highlight some of our more important and exciting recent progress, together with some of the special needs and opportunities, some of the patterns of progress that appear to be emerging for the years ahead.

In the past, studies of the endocrinological effects of environmental stimulation have almost invariably focused upon the ability of a particular situation to bring about an increase in the circulating levels of certain hormones. Little or no attention has been paid to situations which may consistently lower such endocrine levels. We have been attempting to develop experimentally controllable situations of mild stress, and have discovered several conditions which lead to a lowering of plasma hydrocortisone concentrations.

Investigators are also using films in human stress studies. After screening a number of experimental and commercial films, they have found two which produce a high degree of emotional involvement in almost all subjects and fairly often evoke rather intense distress. They have displayed these films to normal control patients and have found consistent increases in plasma hydrocortisone concentrations. For those subjects for whom control levels were also obtained, there is a drop in level during the showing of less emotion involving films (e.g., nature studies).

These findings call attention to psychological conditions under which adrenal hormone levels may be diminished, as well as the more familiar distress conditions under which these levels are elevated and is significant in terms of future attempts to modify the detrimental physiological effects of stress.

Another group of our scientists is collaborating with a group in Puerto Rico in studying the patterns of adolescent adjustment in that culture. This has general importance not only for the light it will cast on our own studies but also because the Puerto Rico youths are going through an adjustment process which is likely to resemble that occurring in many rural agricultural economies as they change over to an industrial pattern.

Research efforts continue to be directed toward the important area of family relationships in schizophrenia. Four of our laboratories are working on the problem from different points of view. One group is studying the developmental aspects, beginning with the newly married couple and following through the birth and development of their children; another is studying the family in relation to the adolescent and his transition from high school to college; another is attempting to delineate variations in parent-child relationships associated with the family's social position and how particular aspects of parent-child interaction affect children's personal development; and another is making a comparative study of family relationship patterns in schizophrenic illness with those in nonschizophrenic psychiatric illness.

These are, by nature, long-range undertakings and conclusive statements are inappropriate at this time: however certain trends are emerging and the work is being reported in scientific papers at various professional meetings on such subjects as: clinical observations supporting the hypothesis that schizophrenic thought disorder may be a learned aspect of family life; the use of family therapy for understanding certain hitherto nondisclosed features of family interaction; the use of art therapy for understanding nonverbal aspects; and a consideration of certain overall structural characteristics of family organization which appear to be meaningful.

Another important area of research is concerned with the mental hospital itself. That attitudes and practices of nursing and attendant personnel affect the patient's progress is recognized. How and why and what goes into the formation of these attitudes is still a moot question. One researcher has studied 1,138 members of the nursing service at St. Elizabeths Hospital and has succeeded in isolating and exploring a series of nurse-patient combinations that serve to reduce or expand psychological distance and thus interfere with or improve the patient's progress. Another investigator working in a mental hospital setting has found that chronic schizophrenics conform to a pattern found by Schacter among normal subjects in which subjects born in earlier birth order were more likely to meet stress in a social manner, i.e., preferring to be in the presence of others, than subjects born in later birth order. This finding has led him to study the relationship between birth order and schizophrenia.

One of our scientists at St. Elizabeths Hospital, where we have basic and clinical scientists working together on pharmacological problems in relation to mental illness, has pursued his investigation of the localization and patterns of discharge of the respiratory and cardiovascular neurones in the brain stem of the cat. Intracellular potentials from individual respiratory neurones in the brain stem of the cat were obtained. These data have amplified and extended the previously published data on the nature of rhythmic discharge of neurones in the so-called respiratory centers. They suggest three factors contribute to produce rhythmic discharge of respiratory neurones: a self-reexciting mechanism within the inspiratory and expiratory networks of the neurones tending to maintain activity within these networks; a self-limiting mechanism tending to limit the frequency and duration of a given discharge sequence; and an arrangement of reciprocal innervation which provides inhibition of one network while the other is active. These findings suggest that an increase in the firing threshold, as a burst of action potentials progresses, may play a major part in bringing the discharge to an end. As a subsequent step, an effort is being made to localize the patterns of electrical discharge of cells related to the central control of blood pressure, and to analyze mechanisms affecting their repetitive discharge. These physiological data will be used in subsequent analysis of the effects of drugs, upon the central control mechanisms governing respiration and blood pressure.

One of the interesting positive findings in schizophrenia research is the recent report of Frohman and Gottlieb at the Lafayette Clinic, who discovered a factor in the plasma which alters the carbohydrate metabolism of red cells. In the past year the laboratory of clinical science invited Dr. Frohman to apply his test to schizophrenic patients and normal volunteers on our wards and to carry out the appropriate analyses in this laboratory. On the basis of blood samples submitted to him from 12 schizophrenic patients and 8 normal volunteers and carefully coded to prevent their identity from being known, he was able to predict correctly in a highly significant number the presence or absence of schizophrenia. In another study, one of our scientists investigating the response of free fatty acids to insulin has found a reproducible alteration from the norm in a significant number of scizophrenic patients. These studies are being actively pursued with the consideration of the many variables involved in an effort to determine to what extent either of these characteristics is basic to a subgroup of schizophrenia or may be the result of adventitious factors.

Another investigator is continuing his study of the intermediate metabolism of tryptophane. Work to date has shown that one possible pathway involves 6-hydroxylation which could result in the production of di-ethyl tryptamine which has psychotomimetic properties. The importance of this finding is that 6-hydroxydiethyltryptamine is the only known normally occurring metabolite the accumulation of which could give rise to psychosislike symptoms. The investigator has improved his method for the determination of 6-hydroxydiethyltryptamine in urine and can now detect small amounts of the metabolite in clinical studies in man and in laboratory animals.

These biochemical studies have been carried on simultaneously with behavioral observations. The animal studies are aimed at establishing the effects of psychotomimetic tryptamine derivatives, and their metabolites, on several types of behavior in various species and at correlating behavioral effects with metabolic variations in the same subject; an attempt is also being made to correlate behavioral effects with chemical structure and the chemical properties of various tryptamine derivatives. The early findings in rats have been confirmed and extended to both monkeys and pigeons. It was shown that the dose required to elicit a significant effect on performance was lower for 6-hydroxydiethyltryptamine (the major metabolite of diethyltryptamine) than that for the parent substance (diethyltryptamine). Substances closely related in chemical structure to diethyltryptamine which are 6-hydroxylated (for example, a-methyltryptamine) were found to have behavioral effects in rats and monkeys, whereas other structurally related substances (such as dihexyltryptamine) which are not hydroxylated exerted no behavioral effects. The compound, a-methyltryptamine, which has a slower rate of hydroxylation than diethyltryptamine, also exerts a more prolonged behavioral effect than diethyltryptamine.

In the Addiction Research Center, which is located at Lexington, Ky., the study of addiction proceeds not only toward the clinical pharmacological, physiological and biochemical characteristics of the addict and postaddict but also to his psychological characteristics. The study of addiction involves more than the examination of a few drugs because addiction has its roots in neurotic character disorders. Its thorough investigation will contribute importantly to our understanding of many aspects of human behavior.

Since man is relatively unique in his pattern of susceptibility to addiction, the Addiction Research Center will need to continue to test potentially addictive materials clinically. To improve this program, scientists at the Addiction Research Center have developed new and simplified methods for making quantitative evaluations of the subjective experiences associated with the administration of addicting substances. A still more basic approach to an evaluation of the subjective effects of drugs has been developed by the psychology staff in the center. This involves the taking of inventories of subject responses and behavior which distinguishes different types of addicting and other psychotropic drugs. This is proving to be broadly useful in the evaluation of the psychological modes of actions of all varieties of drugs.

A most interesting new drug (I–K–1) was evaluated clinically during the year. This compound apparently represents the greatest dissociation between pain-relieving qualities and physical addictive properties that has yet been achieved.

The Addiction Research Center is carrying out important neurophysiological studies on animals to determine the influence of particular types of drugs on neuronal circuitry. It has been established, for example, that brainstem mechanisms relating to arousal and alerting, which are powerfully implicated in motivation, involves both muscarinic and adrenergic synapses. These studies are fundamental to insight into the complex interactions between neuroendocrine mechanisms, the central nervous system and drugs which (1) affect both systems and their relationships to each other and which (2) modify subjective states and behavior. Neurophysiological studies were also carried out on the mechanisms of convulsions and delirium following the withdrawal of barbiturates or alcohol.

In the basic research area, other studies are continuing on the mechanisms and pathways by which protein molecules are synthesized biologically. Specifically, the physical characteristics and role of the soluble fraction of RNA (S–RNA) and the nature of its specificity in relation to amine acids coupling with proteins are being investigated. Also under study are the processes of biological methylation which is important because methylation controls the activation and detoxification of many natural and artificial active pharmacological agents. The hope is to understand the processes involved in the enzymatic biosyntheses of methionine which in turn plays a key role in methylation. Understanding the metabolic sequences involved and the conditions obtaining before and during methylation will provide penetrating insight into general mechanisms controlling cellular economy. In a similar way, studies are underway on alkaloid biosynthesis to provide information relating to processes that control the influence of the alkaloids which are powerful pharmacological agents. Certain plant alkaloids appear to be closely related to the adrenal hormones of mammals and to serotonin. Thus, the study of alkaloid synthesis contributes to a better understanding of neurohormones and of the chemically related hallucinogenic materials.

Other studies include biological oxygenation and hydroxylation. The particular pathway being studied continues to be the enzymatic conversion of phenylalanine to tyrosine, a pathway which is defective in a genetically determined developmental mental disorder, phenylpyruvic oligophrenia. Additional study is being devoted to the general problem of cellular differentiation, particularly in relation to the regulatory role of gene products in embryology. The purpose is to obtain a biochemical view into the regulatory processes of genetic material.

Neurophysiology studies on the processes of excitability have recently reinforced the theory that the action potential upon which nerve conduction depends is really an alternation process in which a biologically maintained potential is shifting between a resting and exalted second stable state of the membrane. Progress has been made in establishing the analogy between nerve membranes and physiochemical, electrochemical, and mathematical models. Thus, the formal requirements for a conducting membrane are becoming increasingly satisfactorily understood. Extension of understanding has also been achieved in respect to the electrostatic field forces surrounding single neurons in the spinal cord. These field forces shift during the course of excitation of the cell and play an important role in the synthesis by the cell of multiple conflicting and reinforcing signals arriving within the synaptic region of single neurons. It is through means of individual synaptic contracts transmitting by neurochemical agents, and the electrostatic field forces which encompass its cell body and dendrited that the cell is able to perform functions analogous to a giant computer in its analysis of an immense number of incoming signals and reduction of these into an output of conducted impulses.

Physical chemistry studies have continued on artificial and natural nucleic acids. These are probably the biologically most important molecules in existence and they need to be characterized physically in order to throw light on their functions and on biological problems arising from defective RNA and DNA. Evidence from one portion of this work indicates that the crystalline structure of natural RNA is basically similar to natural DNA. This defines certain structure aspects of RNA which have been in dispute. Rapid advances have been made in the use of dyes bound to complex molecules as a means of determining the rigidity of the molecules, the distance between dye binding sites, and the characteristics of interactions of the dye particles when they are systematically stacked one on top of the other but still bound to the unknown molecules. This work has already yielded fundamental insight into the nature of dye binding and on the basis for changing coloration of light transmitted through a solution containing dye and complex polyanions (metachromasia). It has also forecast vastly speedier and more explicit physical-chemical identification of nucleic acids and other important biological compounds. For example, it has been established that the color of bound dye can be used to determine the degree of denaturation of natural DNA. One can thus watch, through microscopy, the death of a cell by following the changes of coloration of vitally stained nucleic acids. A quantitative method of analysis in the microgram range has been established for nucleic acids, mucopolysaccharido, and synthetic polyanions. Comparison can be made between plant and animal extracts which will help differentiate in a simple manner, the kinds of dye binding sites, their number and location relative to each other.

Further progress has been made toward understanding enzymatic catalysis and toward the definition of the atomic configuration responsible for enzymatic action.

It is hoped that it will be possible to synthesize a model enzyme instead of having to extract them from living tissue. The very difficult task of determining from direct analysis the sequence of amino acids in large protein molecules is being replaced by a theoretical approach which may permit the mass digestion of the unknown protein, the relatively simple chemical identification of fragments produced by this process and the reconstruction of the original total amino acid sequence throughout the length of the protein molecule by means of mathematical computations programed into an electronic computer. This work is being done in collaboration with mathematicians and engineers at the IBM Corp. This potentially fruitful shortcut has been examined from a logical, mathematical point of view toward the development of an experimental design which will vastly minimize the usual experimental effort and which will process experimental data much more efficiently. If this works out as well as it now promises to do, it will cut short years of laboratory effort and make possible the determination of amino acid sequencing in molecules which would be entirely beyond the practicabilities of present research methods.

The foregoing are indicative of some of the diverse research studies underway in our basic and clinical research programs. It is always difficult if not impossible to identify specific research accomplishments in terms of their ultimate benefit to mankind and the brief list of program developments set forth here are only for the sake of illustration. Certain of these program items have, however, been singled out for special treatment in further detail in our research highlights and in separate documents for your possible further consideration (drug addiction, schizophrenia, etc.).

PROGRAM DEVELOPMENT

Elsewhere in this statement, attention has been given to aspects of the various operating programs of the Institute in the fields of intramural research, grant-supported research, training, and professional and technical assistance to the States. In each of these program areas there is obviously attention to program development in the sense of reviewing and assessing present activities, of improving the administration and conduct of the program, and of planning the next stages of development and growth. This kind of program development is a constant concern to every laboratory, branch, and operating program in the Institute.

In all fields of health, however, and particularly in the case of mental health, it is necessary to remain alert to other program development problems. It is important to deal with new and emerging problems, to study the activities of other groups that face problems of a mental health nature, and to study the basic and recurring processes in the community that have mental health impact. The Institute has three major instrumentalities for dealing with these problems of total program development.

The Professional Services Branch assesses emerging problems which are not receiving adequate attention from scientists and from mental health programs. In the last several years, this group has stimulated grant-supported studies in such areas as rehabilitation of the mentally ill, alcoholism, mental retardation, and delinquency. It also studies the mental health role and impact of other community groups and agencies that are themselves not mental health or even health organizations. In this area, contributions have been made in the field of the mental health influences of the school and of industry. Finally, the group deals with many of the normal and continuing functions, roles, processes, and phenomena of our society that are important to mental health and to which mental health programs can make a constructive contribution. Thus, grant-supported studies have been stimulated in such areas as the role of parents and the way in which they can be assisted in the performance of their role, not only with disturbed children but with normal children. The problem of aging and the factors associated with successfully meeting the challenge of old age have been given much attention and study by this group.

It is not possible here to summarize all of the specific accomplishments of this group, but a few of them will suffice to show that this kind of program development leads to progress and a new ability to deal with mental health problems. In the field of the rehabilitation of the mentally ill, for instance, a long series of studies supported by the Institute on a program development basis at the Harvard School of Public Health is reaching the stage of final reporting. This group now has information concerning a large number of discharged patients and their relatives, and the careful analysis of these data is in progress for publication in book form. It shoulld be pointed out that many of the intermediate findings have been published in the literature already. The Hogg Foundation has published "After Hospitalization: The Mental Patient and His Family" as a preliminary summary of these studies. Also, it should be noted that the Institute has completed analyses of 49 rehabilitation projects represented at a conference on studies on psychiatric rehabilitation, held in June 1959, and that the publication of this careful assessment of the field of rehabilitation will be published in the not-too-distant future in book form. The State of California has been conducting studies designed to determine the impact on the families of serious mental illness upon the part of married female patients with at least one dependent child in the home. These studies basically involve the problem ultimately of rehabilitation, but also contribute to an understanding of the effects of mental illness on family life and the techniques for reestablishing the family as a cohesive unit in the community.

It can be said, therefore, that over the last 9 years the Institute, as indicated by these few examples of accomplishment, has done much to develop the concept of rehabilitation, to explore the techniques and problems associated with enterprise in this area, and to report in an understandable way the hopeful and successful approaches to rehabilitation. It should be noted that many States now are devoting a significant amount of their total efforts to the field of rehabilitation of the mentally ill, which is a statement that could not have been made when the Institute, through the professional services branch, began this systematic study of the problem. It can also be noted that much research is now being voluntarily submitted, primarily for mental health project grant support, involving the field of rehabilitation, and it is felt that the leadership role of the Institute in the early initiation of these studies and their reporting has had much to do wih this increased research interest which is being expressed through the very valuable mechanism of mental health project grants.

Program development in the field of alcoholism is designed to aid in overcoming longstanding problems—problems such as inadequate knowledge, some lack of scientific effort in the area, the relatively low prestige accorded workers in this area, and popular misconceptions about alcohol, its use and abuse.

As indicated last year, a Cooperative Commission on the Study of Alcoholism, supported by NIMH funds, has been established. The Commission has recently succeeded in securing a distinguished scientific director, and the Commission, under his direction, has initiated a complete review and evaluation of the entire field of alcoholism. The experience to date indicates that outstanding scientists can be recruited from outside of, as well as from within, the field of alcoholism. Both scientific interest in and the prestige of the field appears to be increasing.

Other research activities are designed to meet specific and crucial needs in the field. One research project is designed to aid in clarifying the basis for diagnosis of alcoholism and other terms descriptive of the overuse of alcohol. This study should be useful both for research and for treatment purposes. Another study, currently being conducted in California, is designed to develop instruments for measuring nonpathological drinking practices, so that baseline data may be gathered. This is necessary in order to determine deviations from normal practices.

The Institute is disseminating information and knowledge through its various consulting functions to governmental and private agencies. In these efforts it is continuing to stimulate research proposals from competent scientists so that alcoholism may eventually be brought under effective control.

Close working relationships have been developed with the North American Association of Alcohol Programs, catalyzing the activities of this organization of official programs and providing excellent communication with the responsible State agencies.

The work on alcoholism to date has clarified many of the problems that need to be attacked. At this point in history the creation of the Cooperative Commission on the Study of Alcoholism appears to be a feasible undertaking, but it would have been quite unlikely to succeed as much as 5 years ago. It is also reasonable to hope that systematic and organized attention to problems of research and teaching in the alcohol and alcoholism field may prove attractive to several major universities, possibly in cooperation with official State agencies concerned with alcoholism, mental health, and other health programs.

Program development in the field of juvenile delinquency has been actively underway only since 1955. It is, therefore, in a less mature stage of development than is the field of rehabilitation, but has still shown substantial development on a number of fronts. Faced with rapid increases in delinquency rates within the last few years, the Institute staff concerned with the problem have deemed it appropriate to launch an attack on both a long-term and a short-term basis. Because of the large number of unanswered questions regarding the extent of the problem, and the numerous distinct processes by which children become delinquent, it was seen that a long-term effort was needed to increase basic scientific understanding of delinquency and of effective preventive and treatment methods. On the other hand, since the problem appeared to be increasing at a near epidemic rate in some areas, it seemed appropriate, on a short-term basis, to assess the effectiveness of current methods of prevention and control and to use current knowledge to devise control programs for areas where local resources and methods seem no longer adequate.

In line with the long-term strategy, approximately 100 projects have been supported in the last few years which were designed to study processes in the individual, in the family, the neighborhood, the peer group, the school, and the wider community which tend to produce delinquency. These projects have already yielded a number of valuable clues as to appropriate types of intervention and appropriate periods in the child's development for such intervention. Following these leads, a number of projects have been supported in which new knowledge regarding processes are being used to try out new methods of prevention and treatment.

As a part of the short-term strategy, projects were launched with the objective of devising methods of classifying delinquents so that appropriate treatment methods would be indicated by the classification. One such project is completing its pilot phase and may, if it passes field tests, provide tools for such classification by court and correctional personnel who are currently, without the advantages of this kind of information, prescribing the treatment or disposition for most delinquents in this country. In addition, a number of projects have been supported which will both demonstrate and evaluate preventive and treatment methods which are strongly recommended by experienced professionals working with delinquents. Thus far, a number of treatment approaches, usually involving a combination of methods, have proven effective even with chronic and seriously disturbed delinquents. Such demonstrations, however, have involved relatively small numbers of cases so that field trials on a larger scale are the next step. Several such field trials are now underway and a number of others will be reviewed in the spring of 1961.

The National Institute of Mental Health has also supported demonstrations and evaluations of training programs for police, probation officers, clergymen, social workers, and mental health personnel. Projects for the training of juvenile court judges are also under consideration. Some of the training programs have proven effective on a pilot basis and larger scale trials of these programs are projected.

Close working relationships have been established with the official organizations in the field, such as the National Council of Juvenile Court Judges and the National Council on Crime and Delinquency, and interested funding organizations such as the Ford Foundation. Here, too, the number of voluntary research applications has increased. The efforts of State and local government groups in this area have grown markedly, partly as a result of the increased amount of delinquency over the last decade and partly as a result of the Institute's interest and activity in this area.

In the field of community functioning and persistent problems of population groups, it is timely to indicate that the Institute's program development activities in the field of aging are also reaching a stage of significant accomplishment. The study of successful aging conducted by the University of Chicago in Kansas City is nearly complete, and it is expected that a volume will be published in the near future under the tentative title, "The Process of Growing Old." This report will represent an organized statement of many of the problems encountered by people as they approach later years, identifying the frequently encountered difficulties and some of the variables which are associated with adequate or inadequate coping with these difficulties. Out of these findings it is known that there will be many suggestions concerning programs that may be conducted by various agencies of the community and of forms of counseling individuals prior to their older years that will assist them to meet old age in a much more successful manner than many people now do. There have been other significant developments in the aging field, one of which involves an international research seminar on the social and psychological aspects of aging held last August in San Francisco with support from National Institute of Mental Health funds. It should be noted that many countries have had an aging problem longer than has the United States, and that it is very valuable to pool the experiences and knowledge gained in other countries with our efforts to deal with this relatively new national problem. For these reasons, last summer's seminar was highly valuable in the development of this field. Institute personnel participated in this seminar and will be involved in the preparation, editing, and publishing of the proceedings in book form.

It is clear that the Institute has succeeded, through its use of stimulated research and through its support of intramural research in the aging area, in interesting many scientists in the study of this field. It now appears that research concerning the problems of aging can be expected to increase, and that persons responsible for services to older people and programs for them will be increasingly supplied over the next several years with important research findings and scientific material that will improve the ability of communities to deal with the aging.

The mental health factors involved in the functioning of important organizational structures within society are well represented by the work that has been done with the schools. The Institute has supported, for several years, intensive research studies of the mental health impact of the school and the schoolroom and of the influences of the family and community upon the school's functioning in this connection. There has also been support of three institutions for the problem of determining the kinds of mental health, behavioral science, and psychiatric information needed by teachers and capable of being presented at the time of original teacher training. The Institute, through its liaison and program development activities, has arranged joint consideration of these problems by the three separate university groups involved in the problems of teacher training content as well as by the group concerned with major research attack upon psychological and mental health effects in the classroom. Last fall, a 4-day meeting of these research and training groups was convened for the exchange of ideas and the development of further steps in the pursuit of these problems. Careful attention is being given to the proper methods for disseminating this information through appropriate educational channels with the full cooperation of the Office of Education and major educational organizations in the United States. It is felt that here, too, it is possible to say that the last 5 years of activity is now leading to a much clearer perception of the mental health problems of the schoolroom and a concern for the mental health of all children, not only those who have shown psychological disturbance and possibly incipient mental illness, as was the case for so many years. The interest of educators generally in this problem and their willingness to communicate these findings to their colleagues throughout the country means, it is felt, that the mental health role of the school will be improved generally over the next several years in a way compatible with its basic responsibilities and modes of functioning, but also based upon sophisticated information drawn from the fields of behavioral science, psychiatry, and mental health knowledge.

The biometrics program of the Institute also offers opportunities to engage in types of studies and investigations that contribute very much to total Institute planning and program development. The ability to achieve this kind of result in connection with the biometrics program lies primarily in viewing the problem of accumulating data about patients receiving psychiatric care, both in institutions and in outpatient resources, in a much broader way than would be required if one were merely trying to count the number of persons involved at any one time or during any one year. As a consequence of an effort upon the part of the biometrics staff to understand the factors associated with the utilization of mental hospitals and outpatient clinics, several approaches have been developed which it can now be reported to have shed a great deal of light upon the problem of mental health care and rehabilitative efforts. Several years ago, it was decided that the kind of information needed is not merely a current enumeration of patients under treatment, but data which deal with the outcome of treatment in mental hospitals of groups admitted within specified periods of time, such as 1 year. Up to this point in history, no systematic record of mental hospital patients had been kept in this way, so that it was impossible to say what percentage of patients admitted during a particular year, classified by age, diagnosis, and other characteristics, would be likely to be out of the hospital, still in the hospital, or deceased after specified periods of 6 months, 1 year, 2 years, etc. It is quite possible, however, to keep records in this way and the Biometrics Branch of the Institute developed the technical facility for doing so and was able to demonstrate its importance by the analysis of the records of the Warren State Hospital in Pennsylvania. These records, which were essentially unique, did lend themselves to this type of utilization. These early studies indicated that over a period of time the probability of release alive after specified periods of time had varied considerably and in particular ways, with subclassifications broken down by age, sex, diagnosis, and other variables. The demonstration that the likelihood of successful treatment in the hospital has varied with time, then, makes it possible to relate these variations to a large number of other factors, such as changes in the method and modes of treatment, the stage of the disease at which hospitalization is accomplished, the resources for aftercare and followup service to discharged patients, and the like.

In other words, while these studies show that changes in the function of the hospital and other factors associated with hospitalization do result in different rates of release alive, it also raises a large number of questions concerning the factors that contribute to these changes. The Institute has continued to study these phenomena and to make additional attempts to isolate some of the factors associated with changing rates of release from mental hospitals. It is very fortunate that these techniques were initiated early enough that it has been possible to study to some extent and in broad terms the effects, for instance, of the introduction of the new psychiatric drugs during the last several years. These studies have indicated not only that some of the phenomena associated with the net decrease in mental hospital population can be attributed to the utilization of these drugs, but also that other factors, such as the development of aftercare rehabilitation programs, have made it possible to release many patients for return to communities where such constructive circumstances exist, patients who would otherwise have had to remain in the hospital.

What is being said, in other words, is that the apparent effectiveness of hospital care programs and the ability to release patients back to the community is a function certainly not only of the procedures used within the hospital, but the resources within the community upon which the hospital can rely in returning patients to their homes and places of origin. Findings of this kind have been very important with respect to the increased emphasis upon the part of many States in developing programs of followup and aftercare for discharged mental hospital patients.

The Institute has formalized this approach through its development of a model reporting area, which has been dedicated not only to the systematization of hospital records, terminology, and reporting procedures, but also to the stimulation upon the part of the States belonging to this model reporting area of research of the kinds just enumerated above and conducted upon an ongoing or prospective basis. At the moment, 22 States have joined the model reporting area, and they account for the administration of approximately 75 percent of the public mental hospital population of the country. With this basis and the indication that additional States will become participants in this activity, it becomes obvious that we will be able more and more to answer questions concerning the probable stay of patients in hospitals. It will be possible to show the effect of initiating associated programs at the community level upon the length of stay in the hospital. This approach can show better than any number of words or any conceptual presentation that the effectiveness of the hospital does rest, in fact, upon a close working relationship with the communities of the area from which it draws its population. It can also indicate clearly that the problem of treatment of the mentally ill cannot appropriately be considered in unrelated segments, such as outpatient care, inpatient care, rehabilitative efforts, and the like.

It appears fair to say that this statistical study of the factors associated with the fate of mental hospital populations is doing a great deal to stimulate the thinking of those responsible for State and mental health programs and for the administration of hospitals and outpatient facilities generally. While this series of findings now has a record of several years, it is timely at this point to say that the development of these programs by the Institute through the usual mechanisms of consultation and Federal-State interaction has been a very effective device for upgrading the treatment procedures of mental patients and for giving hope with respect to the further improvement of the handling of mental hospital patients. It should be clear, for instance, that the problems of estimating the matter of costs and the nature of return per dollar invested now can be handled in a much different way from what it could in the past. This lays a foundation for determining the economic feasibility of programs of patient care and for the evaluation of new types of institutional arrangements, such as halfway houses, day-and-night hospitals, and the like. Such new type institutions obviously cannot be evaluated only in terms of their value for the patients whom they serve, but in connection with their impact upon the total problem of care, their influence upon the length of stay in the mental hospital, and their contribution to the ability of patients to maintain themselves in the community upon return to their families or other independent living arrangements.

The point that is being made here is an important one. Biometrics procedures can either result merely in tabular representations of the provision of psychiatric services, or they can shed considerable light upon the factors associated with the way these services operate and the variables that influence their effectiveness or ineffectiveness, giving rise therefore not only to program activities upon the part of the National Institute of Mental Health but also upon the part of State and other local persons concerned with matters of mental health.

At a somewhat later date, the Institute began to apply the same thinking and procedures for data collection to the functioning of outpatient clinics, with the hope again of finding out what populations were served by these resources, what kind of services were supplied to them, the quantity of services which was utilized by the various groups, and the nature of the result which was achieved by outpatient clinics. It is only now that enough data have been accumulated to indicate that the functioning of outpatient psychiatric clinics can be understood in a way quite different from what was possible at an earlier time. For instance, it has been found that the average patient who is seen in an outpatient psychiatric clinic receives relatively few interviews, the median number being four. Some of these patients need and receive only diagnostic service and some counseling with respect to the handling of the problem. On the other hand, approximately one-half the adults and one-fourth the children are accepted for more prolonged treatment, and even in these cases, the median number of interviews is not extremely large—on the order of 10 to 12. These figures are much smaller than many persons would have guessed in the past, and are optimistic findings with respect to the number of persons who can be seen and dealt with by these resources. The study of outpatient facilities has also been of value in making available for the first time information concerning the percent of time which clinics spend on various kinds of activities, including that which is devoted to the community services activities of clinics as distinguished from their more definitely clinical work with the patients representing the caseload. This figure, which is only at the level of about 6 percent, has been rather stable over the past several years. Perhaps this finding is a little bit disappointing, but its existence and the knowledge of it gives a basis for States and communities and the appropriately interested persons to deal with the problem of whether or not any change in the pattern of distribution of efforts by clinics in this connection should be encouraged. The National Institute of Mental Health cannot, of course, indicate to local and State groups what the proper or optimal pattern of staff effort by these clinics should be but it is very important for the Institute to be able to provide figures which show what the present reality is so that those concerned with the utilization of clinic resources will have a firm basis upon which to consider policy changes or modifications.

The work which is being mentioned here, as indicated above, has been going on for some time, but the organization and presentation of this material in analyzed form has been increasingly achieved in the last few years. A very significant report was recently published in the November 1960 issue of Public Health Reports concerning the functions and activities carried out by a relatively large percentage of all the outpatient psychiatric clinics in the United States.

The application of systematic reporting techniques to outpatient clinics and the development of cohort studies designed to show the way cases received during specified periods of time are handled and their ultimate disposition (analogous to the studies described above for hospital populations) appear to have very great value for refinement in the planning of community mental health programs, not only from the standpoint of effectiveness but also from the standpoint of efficiency and the clear understanding of the economic factors in the provision of these services.

What has been said about the utilization of the biometrics function for program development is only a partial statement of the role of this part of the Institute, which, of course, includes certain operating responsibilities. It is sufficient, however, to indicate that it is a vital aspect of the Institute's activity if we are to have the information for effective consultation with State and local groups through our regional office structure and through our other consultative relationships with key persons in mental health programs throughout the country. It should be clear that close liaison and communication between the biometrics group and the Community Services Branch, as well as those concerned with the problems of training and research, is necessary if the value of these efforts is to be maximally utilized by the Institute and by mental health program personnel throughout the country.

Another device which the Institute has utilized for program development purposes is the Mental Health Study Center, located in Prince Georges County, Md., adjacent to the Washington area. The study center was organized to secure firsthand knowledge of the mental health problems of the local community and of the various indigenous structures and organizations within that community. It is valuable to know what kinds of assistance competent mental health personnel can provide to health officers, physicians, and other health professionals within an area, and to other important community organizations and agencies such as the schools and police department.

The basic purpose of community mental health programs is to improve the ability of all parts of the community to meet the mental health needs of the population. The provision of treatment for those currently in need of professional service is important but it is only a part of an adequate community mental health program. Consequently, the Mental Health Study Center has served an invaluable purpose in giving the Institute an opportunity to see the real values of mental health resources, not only for the individuals receiving treatment, but also for other professional groups and organizations in the community who are contributing to mental health objectives.

This work has been proceeding for several years and it is now possible to report some of the kinds of relationships which develop and some of the kinds of studies and investigations which can be conducted with a resource of this kind and which are dependent upon the existence of such a resource.

The provision of some service is a necessary role which must be played if the other objectives of research and of promoting mental health activities by all parts of the community are to be effected. The study center has been able to develop a very important and effective relationship with the schools in Prince Georges County and was able to initiate, several years ago, a study of reading disability among the children attending the public schools in that area. The findings themselves are of interest and of significance. A great deal of the reading disability was found not to be associated in many cases with intellectual defect as such, but with psychological disturbance among the children that was expressed by an inability to learn to read. It is interesting to note that the occurrence of reading disability is not uniformly distributed throughout the county, but is characteristically shown by children from geographical parts of the area of which the county is comprised.

Findings of this kind are very important because they lead to the identification of areas within the county where child-rearing practices and other factors are apparently being reflected by this kind of disability. The schools have not used these findings to disavow their responsibility. On the contrary, they permitted the Mental Health Study Center to provide instruction a few years ago on a demonstration basis to selected members of the teaching staff in methods of helping children to overcome reading disorder when it occurs. This kind of assistance was viewed as highly successful and valuable, and the schools have subsequently sent additional teachers for training at university and teacher training centers to develop a wider basis of this kind of competence among their staff. Pupil personnel workers within the school system have established very close liaison with the Mental Health Study Center, utilizing it for occasional referrals of individual children in psychological distress but more frequently as a source for consultation and advice on the best way to conduct their own activities to promote mental health among the students.

The Institute, as indicated elsewhere, has been very much interested in the problem of mental health effects of the school, and the study center's operation has permitted the Institute to have a very close relationship with a school system and to understand upon the basis of firsthand experience many of the factors affecting mental health in the school situation. It has also been clear that this kind of assistance to a school is nonintrusive and does not appear to school personnel to be controlling with respect to the educational activities of the school as such, but helpful in the total problem of educating children and dealing with their problems as they develop during school years.

The actual study of reading disability has been of great value and represents a significant contribution to this problem, but from the Institute's viewpoint this enterprise has indicated that properly oriented mental health personnel can in fact be very helpful to the administrative and teaching staff of a school system. It is hoped that the consultation activities of the Institute and the disseminaion of findings of this kind will eventuate in the course of time in similar assistance to school systems throughout the country upon the part of local mental health personnel in a large number of communities.

The study center has also been able to develop a good relationship with the police department and to consult with them upon the problems of the proper handling of all children who are apprehended by police officers, including those who must be referred to the courts. It is worth noting that some of the staff of the Mental Health Study Center have had the opportunity to work with the police to the extent of accompanying them in squad cars both during daylight and night hours, and to discuss with them on the spot the nature of the problems that they encounter. Again, it is felt that this kind of relationship with the police department is not intrusive with respect to the proper conduct of law enforcement, but highly valuable to the police who have a sincere interest in dealing upon a constructive basis with children who are apprehended. The work with the police department has also resulted in very close working relationships with parole officers who are concerned with children who are under remedial programs as a consequence of law violation. The staff of the study center has been interested in the other activities of the Institute in the area of juvenile delinquency, and increasingly close relationships are being developed between the study center staff and the Professional Services Branch, which has the major responsibility for the augmented effort of the Institute in the field of juvenile delinquency.

The health department, of course, represents a natural ally of the Mental Health Study Center, and a great deal of progress has been made in working with this part of the county government. Among other things a joint program in alcoholism-control has recently been initiated by the health department of Prince Georges County in close cooperation with the Mental Health Study Center, and it is fair to say that probably this program would not have developed if the resource of the study center had not been available to the health officer in connection with the effort. Here again, it is hoped that the example of collaboration between a mental health resource and the public health activity of a county will result in its replication and utilization in other places in the country.

During the time that the Mental Health Study Center has been in existence, Prince Georges County has increased greatly in population and has become much more metropolitan than it was at the time of the establishment of the study center. It would appear that the center's ability to provide consultation and assistance to the health department, police department, and schools concerning mental health activities has enabled the county to remain capable of handling in a fairly adequate manner many of its mental health problems. It is true that this county, like all others in the country, needs additional mental health resources. However, it is important that an organization supplying a relatively small amount of actual clinical service appears to have helped the county deal with its mental health problems through a variety of its resources, rather than depending upon the mere augmentation of clinical time and personnel to deal with cases after they become highly symptomatic. It is impossible to say on a quantitative basis how much preventive work has been accomplished, but it appears quite clear that the center has had not only a value for promoting clinical service but has played a preventive role within the county.

Plans are now being made to improve the staffing pattern of the study center by adding personnel who will enable the group to undertake systematic epidemiological studies and the assessment of demographic factors associated with mental health, mental illness and the need for service. Many of these problems must be solved before communities throughout the country, either upon the basis of their own resources or with the aid of State programs, can efficiently and effectively meet the mental health needs of their communities. In other words, the Mental Health Study Center is producing very gratifying understandings of the relationships that can and should exist between mental health personnel, as such, and other groups within the community that can contribute to the mental health welfare of the population. While the study center has always been research oriented, present plans call for an increased emphasis in this area and the hope is that the next few years will increase greatly the amount of information that will be developed through this resource and that can be made available to States and communities throughout the country.

It is always difficult to look back at the past decade, or even at the year just past, and pick out or identify their most important aspects in terms of progress. And, of course, it is even more difficult to predict with any degree of accuracy the anticipated progress of the future. Nonetheless, I have attempted to highlight some of our more important progress, some of our more important leads, and some of our perceptions in terms of the future. The past years have been full and challenging and I feel that we have moved forward on many fronts. And, in terms of the future, I am sure that we can look ahead to continued forward progress in the years ahead.

I appreciate the attention that the committee has given to this presentation and I shall of course be happy to elaborate on any item of interest to the committee.

CONCLUSION

The amended request for 1962 is $88,324,000 as compared with the adjusted appropriation of $95,603,000 for 1961. This allowance for 1962 will provide for the continuation of 1961 program levels in all activities. An adjustment downward of $11,114,000 reflects the nonrecurring adjustment of project period starting dates of training grants. The increase of $6,813,900 will provide for some increases in research grants; in direct research, the increases will provide for a rounding out of the cooperative research program at Saint Elizabeths Hospital, initiation of a research program in the socio-environmental factors relating to addiction, expansion of the biometrics research program with emphasis on the research relating to the 1960 census, and for certain mandatory and program-related costs; in the review and approval of grants, and administration activities, the increases will provide for staff expansion, to better service and direct the Institute programs.

This request for 1962 is distributed among program activities as follows:

Grants:	
Research	$36,480,000
Fellowships	2,390,000
Training	28,356,000
State control programs	6,000,000
Subtotal, grants	73,226,000
Direct operations:	
Research	9,690,000
Review and approval of grants	1,757,000
Training activities	100,000
Professional and technical assistance	2,803,000
Administration	748,000
Subtotal, direct operations	15,098,000
Total 1962 appropriation request	88,324,000

DECREASE IN PUBLIC MENTAL HOSPITAL POPULATION

Dr. Felix. Again this year I am pleased to report that the populations in the mental hospitals have dropped by another 1.2 percent over 1959. At the close of 1960 there were 535,269 patients in public mental hospitals.

Mr. Fogarty. Is this the fourth year in a row it has decreased?

Dr. Felix. This is the fifth year in a row, sir, that it has gone down. Interestingly enough, at the same time, admissions have increased to hospitals. They increased 4 percent in 1960.

Mr. Fogarty. These past 5 years it has been going down how much?

Dr. Felix. From 0.4 percent, which was the lowest, up to 1.4 percent 1 year. That was the highest.

This is opposed to a trend that was for over 100 years slowly climbing, which I have told you about in years past. This becomes of particular interest to us because of two other things. Admissions to hospitals are increasing each year. They increased 4 percent in 1960 over 1959. They went up from 127.9 persons per 100,000 total population in 1959 to 132.7 persons per 100,000 total population in 1960.

In addition to about 235,000 admissions to public mental hospitals—and I call your attention to the fact this figure I am going to give you is larger—there were 260,000 admissions to psychiatric services of general hospitals. I believe one of the gentlemen on the committee asked the question yesterday about the use of general hospitals. There are 800 general hospitals that now accept psychiatric patients for treatment.

CLINICAL RESEARCH CENTERS

Mr. Fogarty. The general hospitals have been building floors and wings to take care of psychiatric cases, and, at the same time, this clinical center program doesn't include your Institute the same as the others.

Dr. Felix. There are 800 hospitals now. This has gone up quite sharply over the last several years.

Mr. Fogarty. Do you think your program could fit into this center program we were talking about yesterday?

Dr. Felix. Yes, sir.

Mr. FOGARTY. Tell us how.

Dr. FELIX. If you are speaking about the categorical type of center; yes, sir.

Mr. FOGARTY. What about the noncategorical type?

Dr. FELIX. The noncategorical, as I understand it, are general research units in hospitals which will—

Mr. FOGARTY. Isn't that similar to a general hospital?

Dr. FELIX. As I understand it, sir, they are research units in a hospital that are set up to do studies in which patients are used——

Mr. FOGARTY. All kinds?

Dr. FELIX. All kinds. It is, I think, part of the policy involved in this that where a hospital wishes to study psychiatric patients in one of these general units, they can certainly do so. Isn't this correct?

Dr. SHANNON. Yes.

Dr. FELIX. I thought it was. On the other hand, there are certain kinds of studies of psychiatric patients, per se, which are large enough in scope and long enough in duration to go on for many years. So I see a real need for the categorical type of clinical center.

MENTAL RETARDATION

Studies, for instance, in new methods of treatment of psychiatric patients and how this affects certain biochemical processes in the patient; studies of mental retardation—there are one or two places that are interested in developing something of this kind, in which there would be long-term studies of a variety of types of the mentally retarded. This will include everything from metabolic studies of not only phenylpyruvic-oligophrenia, about which you know, but other studies of such conditions as galactosemia and another called maple sugar urine disease. About all we know is that these children are defective and that their urine smells like maple sugar. As to why this occurs has to be worked out.

But in addition to this, there needs to be studies of the training——

Mr. FOGARTY. While we are on the subject of mental retardation—it seems to me that we have kind of leveled off on this push to do something about the mentally retarded.

Dr. FELIX. I wouldn't say we have leveled off. The expenditures in my Institute in 1960, including research, training, State control programs, and our own intramural research, were at the level of $2,676,000; and in 1961 it will be at the level of $3,600,000.

Mr. FOGARTY. That is not really pushing it very hard.

Dr. FELIX. That is a $1-million increase.

Mr. FOGARTY. But you do not think that is enough, do you?

Dr. FELIX. I suppose everything is relative.

Mr. FOGARTY. What do you think we ought to be spending in this field in your Institute?

Dr. FELIX. I think it depends on how rapidly the program can develop. We are working with most places in the country which show any promise at all of developing programs. Many of these now have grants from us, either for training people to deal with the retarded or to do research in this area. It takes some time to enlarge a program. I don't have the graph here of what this increase has been over the years.

PRESCHOOL DIAGNOSTIC CENTERS

Mr. FOGARTY. Take, for instance, preschool diagnostic centers. Are they supported by grants from you or from the Neurological Institute?

Dr. FELIX. This is a program, as you know, that is jointly supported by the Neurological Institute and us. Some of these may be by them, and some may be by us.

Mr. FOGARTY. Are these preschool diagnostic centers for mentally retarded and cerebral palsy children working out as you expected? Are they doing some good?

Dr. FELIX. Yes, sir; I am quite sure they are.

Mr. FOGARTY. Do you think they should be expanded?

Dr. FELIX. I think as rapidly as this can be done, they should be expanded.

Mr. FOGARTY. We have one in Rhode Island, but it is not nearly big enough.

Dr. FELIX. There is another program in Rhode Island in which we are very interested, which consists of a program not only of diagnosis but of counseling with the parents of retarded, assisting them to know how best to handle the youngster and to work with him after the diagnosis has been made.

Mr. FOGARTY. I think that is a wonderful one, too. We have had a hard time getting it in satisfactory condition. It really isn't yet. But what about the preschool diagnostic center?

Dr. FELIX. The last information I had, it is doing very well. It is a very satisfactory program.

Mr. FOGARTY. You have had more up-to-date information than I have had, I guess. According to the last information I had, the place they were in needed painting and fixing up: but that is no fault of yours. The State department of health furnishes the facilities. Parents have written in to me finding fault with the type of building they have to operate in and the lack of facilities, and saying they should have a building of their own. But that isn't your fault or responsibility.

Dr. FELIX. This is a shared responsibility.

Mr. FOGARTY. I wish you would take a look at it, or have someone take a look at it, and give us a good honest appraisal. If the State is at fault, I would like to know it.

Dr. FELIX. Yes, sir.

Mr. FOGARTY. I think the State could be doing more in this area than it is doing.

Do you think these preschool diagnostic centers are worthwhile?

Dr. FELIX. Yes, sir; I do.

Mr. FOGARTY. Do you think they could be expanded?

Dr. FELIX. Yes, sir; I do. I think that they can be expanded. We are seeing more of these all the time. I think it is quite important that these youngsters be identified as early as possible so that the maximum amount of rehabilitation, or habilitation, can be made effective. They can be put into special preschool and early-school placements geared to their mental ability.

Another thing that this does, of course, is, by identifying them early and working with the parents, one is able to get the parents to accept retardation in a way so that they will work constructively with the youngsters.

Mr. Fogarty. Also hasn't it been a fact that the wrong diagnosis has been given in some instances, and it has been found in these clinics?

NEBRASKA PROGRAM

Dr. Felix. That's correct. We have a number of reports on this. In one State they now have a policy, a rule, a regulation, a law—anyway, all children who are to be considered for admission to the training school for the mentally retarded in that State must clear through the university department for diagnosis and evaluation.

They are finding a significant number of these—I don't have the exact percentage, but I can get it for you——

Mr. Fogarty. What State is that?

Dr. Felix. Nebraska—who are not retarded, although they appear retarded. They are actually psychotic children. Of course they need an entirely different kind of treatment than would retarded children. These are screened out and treated quite differently than they would be if they were retarded.

Mr. Fogarty. I would like you to tell us more about that program. If you don't have it here, you can get the information and place it in the record.

Dr. Felix. All right, sir.

(The information requested follows:)

Pilot Screening Treatment Unit for the Mentally Retarded

This project was initiated in 1958 and is committed for support (by the mental health project grants program) through 1963. A pilot screening treatment unit has been established as a facility for the diagnosis and treatment of preschool children whom the State considers mentally retarded. Children up to 12 years of age are examined. The unit consists of outpatient, day-patient, and inpatient facilities, including a specially designed nursery.

All patients in the State under the age of 12 who are committed as mentally retarded are examined. Further, an increasing number of patients are being referred by physicians prior to commitment.

During the first 30 months, 233 children diagnosed as being retarded by the referral source were evaluated and/or treated; 95 were studied as outpatients; 122 as inpatients; and 16 as both outpatients and inpatients; 37 were found not to be mentally retarded; 30 were diagnosed as having mild retardation; 33 were moderately retarded; and 75 severely retarded. Of particular interest were the 51 instances in which it was unable to clearly establish the degree of retardation without observation over and extended period of time. A followup procedure has been initiated and these patients are being reexamined at regular intervals. About half of the patients found to be not mentally retarded were suffering from slow maturation due to emotional deprivation. It has been found necessary to expand the treatment services for emotionally disturbed children because of the number found in this study.

Among the cases were seven of cranial stenosis. Neurosurgery has been resorted to with definite results in one early case.

Each child is examined independently by a child psychiatrist, neurologist, pediatrician, and a clinical psychologist. Pertinent laboratory studies, including routine electroencephalograms, are carried out. Each home is visited by a psychiatric social worker.

Experience on this project to date suggests (*a*) that a significant number of children being committed to institutions need not be institutionalized; (*b*) that comprehensive interdisciplinary participation is often necessary to establish a diagnosis; (*c*) that with early diagnosis and suitable facilities successful treatment of many children labeled retarded can be accomplished; (*d*) that emotional deprivation syndrome, childhood psychoses, and sundry organic states too frequently are diagnosed as mental retardation; (*e*) that the inclusion of a special unit for mentally retarded on a medical college campus stimulates students and faculty interest in mental retardation; (*f*) that followup studies initiated promise valuable longitudinal data.

Mr. FOGARTY. What other programs like this which are new are being developed at this time?

SCREENING FOR PHENYL-PYRUVIC-OLIGOPHRENIA

Dr. FELIX. We are about ready to start, hopefully sometime in the next fiscal year, a mass screening program for phenyl-pyruvic-oligophrenia. We have enough information now through the basic research and the other research that has gone on. A small piece of properly treated paper is placed in the diaper of these babies so that it becomes saturated with the urine. This treated paper is mailed into a central place, where, by means of a simple chemical test, they can identify the presence of phenyl-pyruvic acid in the urine.

Mr. FOGARTY. How?

Dr. FELIX. They can identify this at 2 or 3 days of age.

Mr. FOGARTY. I mean, it could be done in a hospital as a standard procedure?

Dr. FELIX. Yes, sir. What we want to do is to apply this, beginning with one location—and perhaps going later to two or three places in various parts of the country—large communities in which every youngster born is so tested.

Mr. FOGARTY. Why wouldn't it be a good idea to apply it in some of these hospitals where the perinatal study is going on, like the Lying-In Hospital in Providence?

Dr. FELIX. There is no reason why we couldn't.

Mr. FOGARTY. It is one of the best in the country, isn't it?

Dr. FELIX. That is right. There is no reason why we couldn't. We haven't settled on any place.

Mr. FOGARTY. This hospital is working in cooperation with other hospitals on this particular project.

Dr. FELIX. The interesting thing about this is that these children are identified and they are put on a phenyl-alanine-free diet. It looks now as though sometime between 3 and 4 years of age they can be taken off of this diet and put on a regular diet.

But whatever changes would have taken place, they are past that vulnerable period. This, we feel, will save a lot of children from this type of deficiency.

Mr. FOGARTY. I think that is worthwhile. Do you need any more money than what you have in your budget to get this going in 1962?

Dr. FELIX. We don't want to start this with every hospital now. We want to do a field trial or two on this first. There may well be flaws in this. This has been done in small groups and very carefully selected places. We are now ready to put it out in the field and try it and evaluate it in two or three places.

Before we broadcast this to the country, we want to be very sure that it is accurate and effective. If it is not, it would be a waste of money to do it. So at this stage what we want to do is to try it out in two or three communities.

Mr. FOGARTY. Do you have plenty of funds in your 1962 budget to try it out in as many communities as you want to?

Dr. FELIX. The budget before you contemplates doing this, yes, sir.

Mr. FOGARTY. In how many hospitals?

Dr. FELIX. Maybe several hospitals; but it will be in two or three communities, two or three cities, which will mail these test strips in to a central place. This is not an expensive procedure. The actual setting up of the testing facilities, once it is done, can handle a large number of these.

Mr. Fogarty. What else are you planning that is new?

DEVELOPMENTS IN THE STATES

Dr. Felix. Part of this Dr. Masland will be able to report on. I might give you some of the developments in this area in several of the States. You might be interested in this.

In New York the State Department of Mental Hygiene has set up an Office of Mental Retardation as part of the department. This is a formal unit now of the department to develop services for the retarded.

Mr. Fogarty. I think some others have done that, too. I think Connecticut has done that.

Dr. Felix. Yes, sir. In Illinois they have set up a Section of Mental Retardation in the Department of Welfare. In Connecticut the two institutions for the mentally retarded have been brought into the Division of Mental Hygiene in the State Bureau of Mental Hygiene. In Delaware they have now day-care centers, as you know, for the mentally retarded. They receive patients up to 21 years of age in Delaware.

In Massachusetts they are now operating 27 nursery centers or preschool mentally retarded. In Ohio the State-supported schools for the children whose mental retardation precludes attendance in regular public schools are being handled in special classes. These special classes have increased in that State from 220 to 469 over this last year. In Illinois, New Jersey, Minnesota——

Mr. Fogarty. You can give those others for the record, if you wish.

Dr. Felix. All right, sir.

Mr. Fogarty. Give us a complete statement on this.

Dr. Felix. Yes, sir. There is a brief statement by Dr. Masland and myself, a joint statement, of which I have just a piece here, which I could submit for the record.

Mental Retardation

THE PROBLEM

Mental retardation is one of the Nation's most serious health, education, and public welfare problems. Due to the increased birthrate, a decrease in infant deaths, and a longer lifespan resulting from medical advances, the total number of persons who are mentally retarded is growing. Each year, 126,000 mentally retarded children are born and it is estimated that there are today some 5 million mentally retarded persons in the United States.

Only 4 percent of the total number of mentally retarded persons are institutionalized. Of these, 160,000 are in State schools and hospitals for the mentally retarded. Another 35,000 are in hospitals for the mentally ill, and 8,000 are in private institutions. The reported cost is a quarter of a billion dollars a year for those in State institutions. The amount expended in private institutions and by individual families and communities for those not institutionalized is unknown.

NEUROLOGICAL RESEARCH ACTIVITIES

The National Institute of Neurological Diseases and Blindness has an active program of research relating to mental retardation and related neurological and sensory disorders of infancy and childhood both at its Bethesda laboratories and through grant-supported research centers throughout the country. The amount expended for research in this field has increased from $6 million in

1959, to an estimated $10,349,000 for fiscal year 1961. Much has already been accomplished in certain areas, such as kernicterus, cretinism, and phenylketonuria, but much remains to be done.

Approximately 25 percent of the Institute's research appropriation is devoted to this area, the major focus of which is centered upon the collaborative project on cerebral palsy, mental retardation, and other neurological and sensory disorders of infancy and childhood. The project recently completed its second year of operation, after 2½ years of intensive preparation. The research developments are discussed in the special report, "Perinatal Studies."

There are a number of specific projects in this field in addition to the abovementioned long-term project. At Bethesda, the Institute's research projects include microscopic and chemical studies of the brain and central nervous system. Also, in the neuropathological laboratories, various studies concern gross and microscopic examination of the brains of children and adults known to have suffered from mental retardation. These observations in adults and children are being paralleled by animal experiments in which deliberate efforts to produce a mentally retarded animal have been undertaken.

There has been further elucidation of certain diseases responsible for mental retardation. Additional new forms of inborn chemical disorders have been demonstrated, and for one (maple sugar urine disease) a promising dietary therapy has been developed.

A serious problem relating to the conduct of research with severely neurologically damaged children results from the fact that many of them are under custodial care in isolated institutions for the retarded. This year, the Institute has organized a survey group to help plan and recommend means of strengthening research activities in such institutions.

The grant-supported projects include studies on the chromosomes of Mongoloids, the toxic and metabolic deficiency disorders, certain developmental defects, and other studies on mental retardation and related neurological disorders. Chromosomal defects have also been found in a number of forms of mental retardation in addition to Mongolism.

MENTAL HEALTH ACTIVITIES IN RESEARCH, TRAINING, AND PROGRAM DEVELOPMENTS

In reporting research relating to mental retardation conducted at the National Institutes of Health, it should be noted that the programs of the National Institute of Mental Health in this field cover four general areas: contributions to basic knowledge through research, development of new types of services through experimental projects, increase in the numbers and competency of professionals in the field through support of training, and improvement and expansion of service programs through technical assistance and grants-in-aid to States.

Approximately 60 research projects in or immediately related to mental retardation are now being supported by the National Institute of Mental Health. The increase in this Institute's activities in this field is indicated by expenditures of over $2 million in 1959, to an estimated $3,581,000 for fiscal year 1961.

Much of the basic research conducted by this Institute at Bethesda is of direct relevance to mental retardation. Typical of research in the biological areas is the wide array of projects concerned with phenylketonuria. Biochemists are examining the metabolism of the phenylketonuric child in relation to the child's total growth and the function of the excessive accumulation of phenylalanine.

A major project is the revision and standardization of scales of infant and child mental and motor development up to preschool age. The study of mental subnormality in younger children has to date been severely handicapped by a lack of adequate baseline data on the normal child for purposes of comparison.

The new Biosocial Growth Center is conducting a series of studies of parents and children. Stress is placed on psychological factors and on patterns of neuromuscular behavior in the infant and young child. The Institute is also conducting a basic study of family relationships as they differ in the various socio-economic classes.

In the psychological and social area, the National Institute of Mental Health is supporting a number of studies of learning in the mentally retarded. Attention has been focused on how little is really known in detail about the socialization of the child in our society. The study should make a real contribution to understanding child development and normal educational processes. Research is also being supported on the processes of decision and effects of institutionalization of the retarded on both the child and his family; also included is examination of such factors as differences in speech patterns in the institutionalized and noninstitutionalized child.

Under the program of mental health project grants, the National Institute of Mental Health supports demonstration, experimental, and pilot studies related to the care, treatment, and rehabilitation of the mentally retarded. Attempts are also being made to develop and refine screening procedures for detecting mental retardation at earlier ages. The Institute is presently a central point for the collection of data throughout the country on patients resident in institutions for the mentally retarded.

Other efforts of this Institute include support for the professional training of persons in the basic mental health disciplines such as the training of phychologists with special competence in mental retardation. The National Institute of Mental Health also maintains a consultant staff in each of the eight Department of Health, Education, and Welfare regional offices throughout the country to provide professional and technical assistance to a wide variety of programs in all of the States.

FUTURE OPPORTUNITIES

Throughout the life of a mentally retarded person, there are many problems to be solved. In some cases if causes are determined early enough, many of the problems can be prevented. For the others, early home care, health and welfare programs, special education, vocational guidance, and other assistance can help these persons function better and decrease the effects of the retardation.

Research in this field requires close cooperation between the two Institutes and among the several institutions involved throughout the country. A wide range of disciplines and areas of interest are represented in the problems as approached by both Institutes. The disciplines involved include: genetics, epidemiology, statistics, psychiatry, psychology, sociology, obstetrics, physiology, pediatrics, and neurology.

Neurological research is approaching the problem through five major avenues: an evaluation of causes originating during pregnancy and early infancy; studies in heredity; investigation of jaundice, asphyxia and injury of the newborn; detection of biochemical ailments causing retardation; and the relation of encephalitis and other early infections to mental retardation. Mental Health research projects range from studies of purely organic factors to psychological and social aspects of emotion and learning in the retarded, and from basic research on causes of retardation to the development of new procedures for detection and treatment.

It is only within recent years that there has been a concerted effort to meet the problem. Many private agencies, voluntary health associations, State governments, along with the Federal Government are now working on it. Many believe that the hope for the future lies in prevention of the disorder through medical research.

Table of obligations

	Actual, 1960	Estimate, 1961	Estimate, 1962
National Institute of Mental Health	$2,676,000	$3,644,000	$4,882,000
National Institute of Neurological Diseases and Blindness (includes cerebral palsy, perinatal studies, and related neurological disorders of childhood)	8,231,089	10,349,000	10,751,000

Mr. FOGARTY. Go ahead with your statement.

CHANGING NATURE OF HOSPITALIZATION

Dr. FELIX. I have told you about the admissions. I should point out the reason the population goes down is that the release rates are increasing more rapidly than the admission rates. The release rates in 1960 increased 11 percent over the release rates in 1959.

Mr. FOGARTY. What do you mean by "release rates"?

Dr. Felix. The way we calculate this is the number of people released from the hospital alive, less the number of people who had been released and are returned, as opposed to those who come in for the first time. This gives you a net release figure. These are the people who go out and stay out.

Am I making myself clear? If I send five patients——

Mr. Fogarty. The release rate, then, means those who are going out and not coming back, which is going up; whereas in the last 2 or 4 years many of these who have been released were coming back?

Dr. Felix. That is correct. The reason for this is the increase in followup facilities, clinics, and other facilities in the communities; the number of physicians who are now able to handle many aspects of the mentally ill person, including their drug dosage and evaluating what that should be.

But this isn't the whole picture, Mr. Chairman. On an average in 1960—I have given you the figure for the end of the year—but on an average day in 1960 there were 539,000 people in mental hospitals. But in addition to this, taking into account those who have gone in and gone out during the year, the public mental hospitals in this country cared for 1,350,000 people in 1960.

PYSCHIATRIC OUTPATIENT CLINICS

This is how many people were patients in the hospitals at some time during the year. But this isn't all. In addition to this, 510,000 people were cared for as outpatients in clinics over the country. This has been rising each year. There has been a threefold increase in 13 years in outpatient clinics. Every State now has such clinics. This has become so important that 23 States have designated special staffs in their central office to expand and develop and improve this aftercare program.

Mr. Fogarty. What does Rhode Island have in the area of clinics for the mentally ill?

Dr. Felix. I don't have that with me. I could give you some of them, but I am afraid I will miss some.

Mr. Fogarty. I didn't think they were doing very much in that area.

Dr. Felix. Butler Health Center is doing quite a little bit.

Mr. Fogarty. Do you call Butler a clinic?

Dr. Felix. It is operating as a clinic, as well as an impatient department. Because of this large center that they have developed there for a variety of services for the State of Rhode Island—welfare, retarded, the mentally ill, all of these others—much of what is going on at Butler Health Center is in fact an outpatient type of operation in which the people are not resident there.

We were wondering how successful these outpatient clinics were. We did an 18-State survey—representative States, large and small, north, south, east, and west—and we found in that 18-State survey only 8-percent of the patients who came in for outpatient care were referred on to inpatient care, which I think is pretty good. There are a lot of reasons why this can be.

NEW PATTERNS OF CARE

There are a number of different kinds of so-called outpatient programs and short-term care programs to take care of the acutely ill. I have spoken about the short-care program in the general hospitals, for example. Seventy-six general hospitals in the United States—general hospitals, now, mind you—have day-care programs for psychiatric patients who do not remain overnight. They come in in the morning. They get whatever treatment, rehabilitation, they may need. They go home at night.

Fifty-three general hospitals have night-care programs, in which the person works during the day or is gone away from the hospital during the day and comes back in at night.

VOCATIONAL REHABILITATION

In addition to all of this, I certainly want to pay tribute to a wonderful job that the National Office of Vocational Rehabilitation has done. The Federal-State combination of vocational rehabilitation services in this area increased the number of mentally ill who were rehabilitated by over 120 percent last year, and 4,000 such people were put into gainful employment as a result of this program. It was even greater—I don't have the exact figure—but the number of mentally retarded who were put into gainful employment in 1960 over 1959 increased 314 percent.

Mr. FOGARTY. After considerable prodding by this committee.

Dr. FELIX. I wasn't aware of that. I just have the data here, Mr. Chairman.

Mr. FOGARTY. We finally convinced them that they ought to spend more time on these cases; they take more time.

CARE FOR EMOTIONALLY DISTURBED CHILDREN

Dr. FELIX. A few examples of some of these devices which are working: In Tennessee they have a mental health clinic that is experimenting with day-care schools for psychotic children. These are not retarded; these are psychotic children, schizophrenic children. New York has two experimental day treatment centers for emotionally disturbed children, the predelinquent children.

Mr. FOGARTY. Is a child with schizophrenia a psychotic child?

Dr. FELIX. Yes, sir, schizophrenic children are psychotic. There are other types of psychoses also. This is not a new concept. We were using this concept and were diagnosing and treating schizophrenic children as far back as 1936 when I was in training at the Emma Pendleton Bradley Home in Riverside, R.I., when Dr. Charles Bradley was in charge there.

This phenomenon was described in great detail many years ago by Dr. Leo Kanner of the Harriet Lane Clinic of the Johns Hopkins Hospital. These children are in fact schizophrenic and they fit all the criteria of schizophrenia. I have seen these children as young as 4 or 5 years of age, and they are a pitiful thing to see.

EMERGENCY PSYCHIATRIC SERVICES

In both South Dakota and in Boston—in Aberdeen, S. Dak., and in Boston they have established emergency psychiatric services which go to the home on emergency call and deal with the problems right there.

In a study done in Boston of 75 families so visited, only 8 families had any member of that family who had to be referred for inpatient treatment. Before, under the old system, when they would become upset they would call the police or someone and in all probability all of them would have gone to the hospital. Only eight families had any member at all who went to the hospital.

NEW PATTERNS OF WARD ORGANIZATION

Another device which to me is very exciting: In Iowa they are now admitting patients to the State hospital at Clarinda to units which serve the county from which the patient comes. People are kept together by county, or maybe a couple of counties, in one building. The same people who treat these patients in the hospital follow them back home, carry through on followup care and work with the families.

MENTAL RETARDATION

The program which I think is going to be a model to other localities is a consultation and referral service for the retarded, including giving parental advice, in Providence, R.I. I might say that as of this morning I had word that some of the problems there are working out very nicely. It looks as though it is going to go forward, and we are interested in working with them and giving them assistance. I think this is going to work out.

Until it has gone a little further, I can make nothing but a promise; but it looks very hopeful to us this morning.

EMOTIONALLY DISTURBED CHILDREN

There are other States I could mention. I would like if I had time to mention some of the things happening in Delaware, Illinois, New Jersey, places of that nature. In Texas they have started a new system for working with emotionally disturbed and psychotic adolescents which is very interesting. They are bringing them in to the University of Texas Medical Center for a 2-day intensive period of treatment, and then they go back out for 6 weeks, and then they are brought back again.

The whole family comes in for this, so that all the members of the family are involved—2 days, and then they are gone for 6 weeks. Eighty-five percent of these children have shown sufficient recovery that they could return to school and mingle in the community.

This is a big step. Instead of having to take a youngster and put him in an institution, if you can take 2 days out of every 6 weeks and work with him like this, this is a big advantage.

PSYCHOACTIVE DRUGS

You might be interested in some of the things that are happening as a result of the wider application of drugs. At the Manhattan After-Care Clinic in New York they have treated a series of patients who suffered relapses—outpatients—with drugs. They were able to return these patients to work within 6 weeks without hospitalizing them.

Mr. FOGARTY. Are these drugs which have been on the market for some time?

Dr. FELIX. Yes, sir, these are standard drugs—selected drugs. They don't use the same drug on all patients.

In Delaware they have done a 4-year followup study of the patients released and treated with the appropriate drug, and they find that a little over 13 percent of these have relapsed as opposed to 47 percent of those not treated.

NINE-HOSPITAL COOPERATIVE STUDY

We are just now establishing a nine-hospital cooperative study to evaluate a number of these drugs. These are hospitals in various parts of the country. They vary in nature from very fine private hospitals to universitiy psycopathic hospitals to public mental hospitals.

The reason we are doing this is that it has been claimed by some that the better the staff and the better the treatment, the less there is need for drugs; or the drugs are not as effective because patients receive other things in lieu of them. This has been said often enough. But, among other things, we want to test this and see.

If the patients at some of these very good places do as well without drugs, this is something important to know. This is an argument for a different kind of staffiing pattern and a different type of personnel perhaps in some of the other hospitals.

This nine-hospital study, incidentally, among other things, will replicate the Veterans' Administration studies. This doesn't mean that we don't believe their results; it will be a further check. The VA has run now, I think it is six different studies evaluating these drugs. This becomes very important because it has been claimed that the results on the VA patients are not necessarily applicable to the entire country because the large proportion of patients treated in the VA hospitals are a more chronic type of mental illness than what you would encounter in a receiving hospital or an excellent private hospital.

So this will be a check on that and an extension of it, too.

RESEARCH ON STRESS AND COLLABORATION WITH THE HEART INSTITUTE

Of course all of this depends upon—and has been made possible because of—the underpinning fundamental research that has been a part of our program for the years since we have been in existence. I would like to mention one only because of time, but this is one that has particularly fascinated me because it shows, in addition to everything else, the close tie-in between the Institutes at NIH and how similar the problems are which affect different Institutes. This is one in which the Heart Institute has played a great role. In fact, some of the discoveries here were by the Heart Institute.

It has been known for a number of years that emotional stress in man was associated with increased adrenal cortical activity and the adrenal hormones—epinephrine, norepinephrine, aldo-sterone and hydrocortisone, which were poured out in larger and larger amounts, depending upon the degree of stress.

There was a linear relationship between the amount of stress and the amount of the hormones that were manufactured.

We have done a study in the Clinical Center on a group of normal people, psychiatrically normal people, laboring under various degrees of stress, to see what happened. We took one group of normal healthy college students and hospitalized them for about 7 days to 2 weeks.

We found that during the first day or so the level was up a bit because the environment was strange and they weren't quite sure about it, but it tapered off. We took another group of college students who were on the ragged edge of failure, flunking out of school. We noted that as they came closer to the examination period their level went up, until after the examinations, and then it dropped off very sharply.

Then we took another group of healthy normal parents of children who were suffering with grave, very frequently fatal, disease. We found that these people showed very high hormone levels during the period that these children were sick.

Then we took a group of depressed—these were psychiatrically ill—patients whom we saw shortly after some major crises or loss which had precipitated this depression. We found that they had fantastically high levels of these hormones. In fact, these levels were as high as are obtained with certain of the adrenal tumors.

We found as the depression tapered off, the hormone level would drop. Then if they had an exacerbation of the depression, it would go up again.

The Heart Institute has shown that epinephrine, working together with hydrocortisone, mobilizes fat and increases the blood level of some of the fat substances such as cholesterol, the phospholipids and free fatty acid. Our people are speculating that it may well be that there is a phylogenetic reason for this in that animals other than man, when they are stressed, do something involving muscular activity. They fight; they run; they thrash around; they do something. Anyhow, they burn up a lot of energy.

The Heart Institute has also shown that fat is burned as well as sugar, and this is a type of fuel that is needed. The point here that is important to us is that people such as we on this side of the table and you on your side of the table lead sedentary lives from the standpoint of muscular activity.

What happens to us when we are stressed? We pour those hormones out just like every other animal, but what happens to us? We get these high blood levels. We mobilize these fatty acids in the blood. We don't burn them up—the point being that it has been empirically known for years that certain classes of people seem to be subject to certain kinds of somatic diseases. We have often talked about coronary disease as the doctors' disease. The surgeon stands up and operates for hours on end. He may be very stressed. But certainly what he is doing there is not violent muscular exertion.

We are now interested and are working with the Heart Institute to find out what happens to these substances. I think Dr. Watt will agree that they are not infrequently deposited in the blood vessels. They may be mobilized out of the blood vessels again. In other words, it may be moved in and moved out. But does there come a time when one has been stressed long enough that the body economy changes so that this material is no longer moved out of the blood vessels, but stays there, and is this part of what stress does?

"Well," you can say, "this is fine; but what has all this got to do with doing something about it?" It may well be that either through chemical means of reducing the awareness to stress or through psychological or sociological means of reducing stress we may make in our Institute some contribution to some of the problems that are of concern to the Heart Institute.

By the same token, the Heart Institute, as it understands more about this whole metabolic cycle, may very well come up with some answers which will assist us in knowing how to reduce the effects of stress that are seen in our patients.

This discussion is a little longer than I meant to give you, but I really feel, when you think of the high incidence of atherosclerosis, coronary disease, hypertension—things of this nature—that two Institutes working together like this to attack a problem from two different points of view illustrates to my mind the NIH at its very best, and its very best is awfully good in my opinion, in attacking problems of man.

There will be more problems of this kind. We will be working with other institutes, I have no doubt.

Mr. Chairman, that completes any comments I have. The budget before you will take positive steps to reach the goals set forth in the Mental Health Act.

BUDGET REQUIREMENTS

Mr. Fogarty. You almost have to say that anyway, don't you?

Dr. Felix. There are increases in this budget, Mr. Chairman.

Mr. Fogarty. There are some but they do not equal anywhere near as much as many people in your field would like to see.

Dr. Felix. That is quite so.

Mr. Fogarty. We have men come here representing your society and field that say you should have another $100 million.

Dr. Felix. That may well be. I don't know about that.

PERCENT HOSPITAL BEDS OCCUPIED BY THE MENTALLY ILL

Mr. Fogarty. Is it still true that over 50 percent of all the hospital beds are occupied by mental patients?

Dr. Felix. About 50 percent, yes, sir.

Mr. Fogarty. What do we have—about a million beds in this country now?

Dr. Felix. I think so; I am not sure. Is that about right?

Dr. Shannon. Yes.

Dr. Felix. About a million beds. The mentally ill occupy about 530,000 now.

Mr. Fogarty. Fifty percent of them?

Dr. Felix. Yes.

Mr. Fogarty. So it is one of the real problems in health, isn't it?

Dr. Felix. Yes, sir, this is true.

Mr. Fogarty. I understand that tomorrow there is supposed to be a press conference concerning the release of the report by the Joint Commission on Mental Illness and Health, after a 5-year study on mental health. Is that when that Commission was set up—about 5 years ago?

Dr. Felix. Yes, sir.

Mr. Fogarty. What was the original intent of that Commission?

Dr. Felix. I believe the intent, as stated in the joint resolution of the Congress which set it up, was to study the problem of mental illness in this country; to give some determination of its scope; what was being done about it; and what should be done about it; and to make recommendations to the Congress, to the Surgeon General, to the Governors of the States, and I believe to the general public.

Mr. Fogarty. That release will be made, then, Friday, March 24, as I understand it.

Dr. Felix. I understand that is correct.

Mr. Fogarty. There have been advance releases of the report. It is really a book.

Dr. Felix. Yes, sir.

Mr. Fogarty. I have one in my office, but I haven't had a chance to read it because it is about 2 inches thick.

Dr. Felix. That is being published.

Mr. Fogarty. Is that the report?

Dr. Felix. That's the report. Then there is a smaller, boiled-down summary which I am frank to tell you I have not read in detail.

Mr. Fogarty. I haven't seen it. Do you have any copies of it?

Dr. Felix. Yes, sir, I have a copy.

Mr. Fogarty. Would you supply all members of the committee a copy of it?

Dr. Felix. Yes, sir, I will be glad to.

Mr. Fogarty. Will you be able to do in the next year what they think you ought to be doing in 1962?

Dr. Felix. As I have said, I have not studied this, so I am not in a good position to discuss it. I believe, though, that their recommendations go well beyond any one year. Further than that, they go well beyond any activities that are presently authorized by legislation.

Mr. Fogarty. Of course I am just talking now about what is authorized.

Dr. Felix. They recommend increased activities in the area for which we are responsible, yes, sir.

Mr. Fogarty. Refresh my memory now. I think we made an apappropriation for this 5 years ago, to get it started.

Dr. Felix. Yes, sir.

Mr. Fogarty. How much money did we appropriate?

Dr. Felix. $1,250,000.

Mr. Fogarty. I notice that this report, called Action for Mental Health, is to be published and released on April 7 at $6.75, plus postage. That is quite a bit of money for a book.

Dr. Felix. As a part of what the Congress directed, copies of that report will be furnished to those designated in the joint resolution. As

I understand it, a copy of that book will be delivered to each Member of the Congress in both Houses and copies will be supplied to the Surgeon General for appropriate people as he sees fit.

The third group which is to be informed—as I have said—are the State authorities.

Mr. Fogarty. "Congress, Governors, and the Legislatures."

Dr. Felix. That's right; and copies will be made available to them as part of this program.

Mr. Fogarty. Would you put the names of the members of that Commission in the record?

Dr. Felix. I will put them in the record. It is a rather large group made up of representatives of a large number of professional and technical organizations concerned directly or indirectly with the field of mental health, such as the American Medical Association, the American Hospital Association, the American Psychiatric Association, the American Psychological Association, the American Nurses' Association—and that is just a beginning. I think there are 20-some organizations.

(The list of members, and participating agencies, follows:)

Joint Commission on Mental Illness and Health

PARTICIPATING AGENCIES

American Academy of Neurology.
American Academy of Pediatrics.
American Association for the Advancement of Science.
American Association on Mental Deficiency.
American Association of Psychiatric Clinics for Children.
American College of Chest Physicians.
American Hospital Association.
American Legion.
American Medical Association.
American Nurses Association and The National League for Nursing (Coordinating Council of).
American Occupational Therapy Association.
American Orthopsychiatric Association.
American Personnel and Guidance Association.
American Psychiatric Association.
American Psychoanalytic Association.
American Psychological Association.
American Public Health Association.
American Public Welfare Association.
Association for Physical and Mental Rehabilitation.
Association of American Medical Colleges.
Association of State and Territorial Health Officers.
Catholic Hospital Association.
Central Inspection Board, American Psychiatric Association.
Children's Bureau, Department of Health, Education, and Welfare.
Council of State Governments.
Department of Defense, United States.
National Association for Mental Health.
National Association of Social Workers.
National Committee Against Mental Illness.
National Education Association.
National Institute of Mental Health.
National Medical Association.
National Rehabilitation Association.
Office of Vocational Rehabilitation, Department of Health, Education, and Welfare.
U.S. Department of Justice.
Veterans' Administration.

INDIVIDUAL MEMBERS

Kenneth E. Appel, M.D., Philadelphia, Pa.
Walter H. Baer, M.D., Peoria, Ill.
Leo H. Bartemeier, M.D., Baltimore, Md.
Walter E. Barton, M.D., Boston, Mass.
Otto L. Bettag, M.D., Springfield, Ill.
Mr. George Bingaman, Purcell, Okla.
Francis J. Braceland, M.D., Hartford, Conn.
Hugh T. Carmichael, M.D., Chicago, Ill.
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James M. Cunningham, M.D., Dayton, Ohio.
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Neil A. Dayton, M.D., Mansfield Depot, Conn.
Miss Loula Dunn, Chicago, Ill.
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Very Rev. Msgr. P. J. Frawley, Ph. D., New York, N.Y.
Mr. Mike Gorman, Washington, D.C.
Robert T. Hewitt, M.D., Bethesda, Md.
Herman E. Hilleboe, M.D., Albany, N.Y.
Nicholas Hobbs, Ph. D., Nashville, Tenn.
Bartholomew W. Hogan, rear admiral, MC, USN, Washington, D.C.
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Miss Madeleine Lay, New York, N.Y.
Mary F. Liston, R.N., New York, N.Y.
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Berwyn F. Mattison, M.D., New York, N.Y.
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Daniel Blain, M.D., Sacramento, Calif.
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Russell A. Nelson, M.D., Baltimore, Md.
Mrs. Elizabeth H. Ross, Washington, D.C.
Harry C. Storrs, M.D., Hanover, N.H.

Mr. FOGARTY. Is it a unanimous report?

Dr. FELIX. That I do not know either. I have not communicated with them because this was a report to the Congress and to the States as I understood it. I do not know.

Mr. FOGARTY. They haven't been trying to keep you in the dark, have they?

Dr. FELIX. No, sir.

Mr. FOGARTY. Aren't you the president of the American Psychiatric Association?

Dr. FELIX. Yes, sir, that's correct. Five members of our association were appointed as our representatives to negotiate for us. So they will probably give us a report on this before my term of office is over.

RECOMMENDATIONS

Mr. FOGARTY. I don't think I will ask many questions on it because I haven't seen this digest before this morning. It does say on page 33, "How can we catch up?"

> How can we catch up? The cost: Federal, State, and local expenditures for public mental patients' services should be doubled in the next 5 years and tripled in the next 10. Therefore, we recommend that the States and the Federal Government work together toward a time when the share of the cost of the State and local mental health patients will be borne by the Federal Government through Federal grants in aid for research and training.
>
> Congress and the National Institute of Mental Health, with the assistance of the intervening administrative branches of government, should develop a Federal subsidy program that will encourage States and local governments to emulate the examples set by the Veterans' Administration in mental hospitals.

They have several recommendations on a local study level, but I don't see the dollar figures. Here is one:

> Hypothetical cost of Federal-State-local governments for doubling expenditures for public mental patient care in 5 years and tripling cost in 10 years in the proposed matching plan in billions of dollars: Federal grants without local participation, $100 million.

What is your program for 1962?

Dr. FELIX. I am not sure what they are talking about. I think they are talking about State control programs there and assistance in hospital care, are they not?

Mr. FOGARTY. Federal grants without local participation.

Dr. FELIX. I would think that would be title V, the mental health projects program. It wouldn't be the matching program because they say without State participation.

Mr. FOGARTY. It says "Federal grants without local participation."

Dr. FELIX. That must mean some type of a direct subsidy.

Mr. FOGARTY. I realize it will be too big a job to do in time for this record, but after you have had a chance to review these recommendations, I wish you would advise us how far short your 1962 appropriations are in comparison with their recommendations.

Dr. FELIX. All right, sir.

1962 BUDGET ESTIMATES

Mr. FOGARTY. Your adjusted appropriation for 1961 is $95,603,000, and the Eisenhower budget is $82,922,000, or a decrease of $12,681,000. What accounts for that decrease?

Dr. FELIX. Sir, $11 million plus of that are the funds appropriated last year for advance notification of training grants so that we could get the schools on an advanced planning basis. The balance is for various nonrecurring items, which offset the program increases.

Mr. FOGARTY. That brings you up to date now?

Dr. FELIX. Yes, sir.

Mr. FOGARTY. The budget amendment brings the 1962 request to $88,324,000, or a decrease of $7,279,000 from 1961. There is a nonrecurring item of expenses—that is what you just said—of $11,114,000 in training grants. Taking that into consideration, the Eisenhower budget was a cut of about $1.5 million, and the revised budget is an increase of about $4 million. That is not much of an increase.

Also I see the budget shows a big reserve for contingencies in 1961, almost $3 million. What is that for?

Mr. SEGGEL. That is the amount of money in the unprogramed reserve of which we have asked for the release of $1,820,000.

Mr. FOGARTY. You still have $1 million there. You mean you are not going to spend $1 million in 1961?

Dr. FELIX. Some of these are programs which we had developed rather late. I do not believe in my best judgment we could wisely expend that this year—not because the programs won't be underway; but they will not have been underway long enough to have used that amount of money in 1 year.

HISTORY OF 1962 BUDGET

Mr. FOGARTY. Now give us the history of your 1962 regular requests and then the history of your budget amendment. I think we can save time by putting that in the record. Put the complete table in the record.

Every Institute Director will do the same if I forget to ask.

(The requested information follows:)

Development of 1962 budget estimates for mental health activities

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Healh, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$46, 420	−$6, 991	$39, 429	−$890	$38, 539	−$6, 844	$31, 695	$39, 836	−$3, 356	$36, 480
Fellowships	3, 686	−996	2, 690	0	2, 690	−300	2, 390	2, 690	−300	2, 390
Training	37, 300	−8, 944	28, 356	0	28, 356	0	28, 356	28, 356	0	28, 356
State control programs	8, 000	−2, 000	6, 000	0	6, 000	0	6, 000	6, 000	0	6, 000
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	95, 406	−18, 931	76, 475	−890	75, 585	−7, 144	68, 441	76, 882	−3, 656	73, 226
Direct operations:										
Research	10, 425	−430	9, 995	−131	9, 864	−542	9, 322	9, 690	0	9, 690
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	1, 963	−393	1, 570	+11	1, 581	−15	1, 566	1, 959	−202	1, 757
Training activities	298	−198	100	0	100	0	100	100	0	100
Professional and technical assistance	3, 129	−326	2, 803	0	2, 803	−24	2, 779	2, 803	0	2, 803
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	964	−240	724	0	724	−10	714	748	0	748
Total direct operations	16, 779	−1, 587	15, 192	−120	15, 072	−591	14, 481	15, 300	−202	15, 098
Total obligations	112, 185	−20, 518	91, 667	−1, 010	90, 657	−7, 735	82, 922	92, 182	−3, 858	88, 324

PROGRAM REQUIREMENTS, 1962

Mr. **Fogarty**. Also, as I asked last year, Doctor, in your professional judgment how much do you think ought to be appropriated for 1962?

Dr. **Felix**. Well, Mr. Chairman, the budget before you allows for increases. There are increases in the area of research——

Mr. **Fogarty**. You only have an increase of $4 million for all your activities. Tell us now what in your professional judgment you think ought to be appropriated for 1962?

Dr. **Felix**. We could perhaps use some increases in some areas. I haven't given a great deal of thought to this.

Mr. **Fogarty**. Didn't you think I was going to ask you?

Dr. **Felix**. Well, I am up here to support the budget I have before me. It is a forward-looking budget.

Mr. **Fogarty**. That is what you are supposed to do until I ask this kind of a question. Then you are supposed to give us your best professional judgment as the answer.

Dr. **Felix**. In view of the growth the program has made to date, I believe we could use additional funds in a number of the items.

Mr. **Fogarty**. About how much?

Dr. **Felix**. I haven't figured it up, but I would say in total we could use somewhere between $117 and $120 million as a total figure.

Mr. **Fogarty**. You figure it out a little more carefully and put the figure and the details of the program that would cover in the record.

Dr. **Felix**. Yes, sir.

(Dr. Felix submitted the following for the record:)

In my professional judgment an estimate of the amount which could be used in 1962 totals $117,567,000. (More detailed information appears on p. 476.)

TRAINING

Mr. **Fogarty**. There still is a shortage of trained psychiatrists; isn't there?

Dr. **Felix**. Yes, sir.

Mr. **Fogarty**. What are you doing about training?

Dr. **Felix**. I think we have taken a very constructive step, sir, in the last 2 years. The most important step taken in some time was that which the Congress allowed us to do by appropriating funds last year and some the year before—most of it last year—for getting the schools on an advance notification schedule so that they know before the academic year starts what money they are going to have.

This takes them off of the hand-to-mouth existence that they had. They know before the year starts what they can count on. They know how they can recruit for faculty and for students. This was one of the healthiest things that has happened.

Mr. **Fogarty**. How much of an increase do you have in your budget now for training and fellowships?

Dr. **Felix**. There is no increase in 1962 over the 1961 program contemplated here.

Mr. **Fogarty**. Why not?

Dr. **Felix**. This is in the judgment of those who had to view the entire program of the Department and the Service and the Government as a whole. It was thought that this was the wisest way to distribute the funds.

Mr. **Fogarty.** What did you ask for training and fellowships? I have it here. You asked for $37 million in training.

Dr. **Felix.** I asked for $37,300,000 in training, and $3,686,000 in fellowships.

Mr. **Fogarty.** Do you still think you could use that additional money?

Dr. **Felix.** Mr. Fogarty, if there weren't any other parts of the Government other than the National Institute of Mental Health—let me say that first so that you know I am not trying to be unrealistic—yes; we could use this.

Mr. **Fogarty.** Could you use any more?

Dr. **Felix.** I think that these would be about the right figures for 1 year.

Mr. **Fogarty.** What would you do if Congress gave you more than that?

Dr. **Felix.** I would do my very best to see that they were expended wisely and to the best interests of the people.

Mr. **Fogarty.** Congress in the past has not thought too much of the estimates that have been sent up in the annual budgets.

Dr. **Felix.** Oh. Certainly Congress has been——

Mr. **Fogarty.** We have treated this program rather well.

Dr. **Felix.** Certainly Congress has shown a most sympathetic interest and deep understanding. In the House, this committe has had this attitude. This program could not have grown as it has grown had it not been that you and your colleagues on the committee over the years have understood and have had a desire to push this forward. I certainly wouldn't want by what I said to let the impression be left that I thought otherwise, because we could not have done what we have done had you not been not only interested but at times pushed us—and sometimes I wasn't happy when I was pushed, although now I thank you for it.

Mr. **Fogarty.** I think you ought to be pushed a little more. You don't have any increase in training, and that is one of the biggest obstacles in the field of mental health. You don't show any increase at all. That is like going backward, as far as I am concerned.

BACKLOG IN RESEARCH GRANTS

Do you think you will have any approved, unfunded, research-grant applications at the end of 1962 with your present budget?

Dr. **Felix.** If the unprogramed reserves are not released, I would anticipate a backlog in research grants of a little over $5 million.

Mr. **Fogarty.** How much?

Dr. **Felix.** If the unprogramed reserves are not released and we operate on our present available funds, and considering next year's budget as part of this, I would anticipate in fiscal year 1962 an amount of money of a little over $5 million we would be short in grants—approved grants we could not pay.

Mr. **Fogarty.** What would be the total of approved but unfunded research grant applications at the end of 1961?

Dr. **Shannon.** There will be none if the Bureau of the Budget reserves are released, which we anticipate they will be.

Mr. FOGARTY. It has just been brought to my attention that in this table you have submitted to the committee, you say that the number and amount of recommended but unpaid applications from 1961 to carry over to 1962 for reconsideration would be $1,488,000.

Mr. SEGGEL. Mr. Chairman, this was on the basis of $6,782,000 in the reserve for the total National Institutes of Health. As we indicated, we have now requested the release of reserves where required, and wherever funds still exist in the reserve there would be no unpaid approved applications remaining.

So, if the funds are released as requested, we would be able to pay all of those.

Mr. FOGARTY. So you won't have any?

Dr. SHANNON. Not in this year.

Dr. FELIX. If the funds are released.

Mr. FOGARTY. When you made these tables up, you must have figured the Bureau of the Budget wouldn't release this money.

Mr. SEGGEL. Mr. Chairman, at the time these tables were prepared, we had not developed the request for release of unprogramed funds. We submitted this request on the basis of the latest study section figures.

Mr. FOGARTY. You mean you had planned to let these projects go unfinanced?

Dr. SHANNON. No, sir. But we wait until we know the precise dollar value of the funds that we need to pay the projects before we make the request. This is never possible before the latter part of February or the beginning of March. These tables are prepared for the hearings before that time.

Mr. FOGARTY. This is dated the middle of March.

Mr. SEGGEL. I believe, sir, the 1961 table we submitted was dated March 6. We didn't have the request prepared at that time.

Mr. FOGARTY. Well, the March 6 table was supposedly brought up to date on March 14 and it is your table of March 14 that shows that there will be 85 applications totaling $1,488,000 that will be approved but not funded in 1961.

Mr. KELLY. Mr. Chairman, the study sections indicated we needed $18 million, which our earlier projections had not indicated. As soon as this was written up, it was sent to the Secretary and he directed us to initiate action to have the reserves released to the extent necessary to fund the approved projects that couldn't be financed with existing funds.

But the table was made up showing the effect on the basis of the present apportionment before that decision was made.

Mr. FOGARTY. Last year the committee in its report said that it would expect increased emphasis on programs in aging, in alcoholism, drug addiction, and mental retardation. Tell us what you are doing in those fields.

AGING

Dr. FELIX. In the field of aging, our expenditures in 1961 will amount to about $1,800,000. There is a report on this which is a joint report, I think through the Division of General Medical Sciences, which includes our activities with that of other parts of the National

Institutes of Health. I don't know that it is my prerogative to volunteer this. Is that all right?

Dr. SHANNON. Yes.

Dr. FELIX. That can be submitted for the record. It will give you a composite picture of the whole NIH activities in this area.

Mr. FOGARTY. Very well.

(The report referred to follows:)

SUMMARY OF NATIONAL INSTITUTES OF HEALTH (NIH) PROGRAMS IN AGING, 1960[1]

INTRODUCTION

The purpose of this document is to report on the many programs in aging research being supported by the National Institutes of Health, including both intramural and extramural activities. There has been a notable increase in the number of aging research projects initiated during 1960 as compared with previous years.

The three broad areas in which research is being supported are: the behavioral and social sciences, the clinical sciences, and the biological sciences. These research activities seek to provide the answers to questions relating to the older person's mental health, physical well-being, and the very basic questions relating to the exact nature of the biologic processes and their relationships with disease..

INTRAMURAL ACTIVITIES

It should be recognized that all NIH research projects will produce information accruing to the benefit of all age groups including the older age group. The chronic disorders such as heart disease, cancer, arthritis, blindness, mental illness, and metabolic and dental disorders in which the seven Institutes carry on research, all affect the older age group in varying degrees, as do the infectious diseases which are also the subject of continuing study..

In addition, there are two intramural programs devoted especially to aging. These are the section on aging, National Institute of Mental Health, and the gerontology branch of the National Heart Institute.

Section on Aging, National Institute of Mental Health

This unit, established in 1953, is organized to secure, through experimental investigations of the behavioral capacities and physiological status of animals and humans, an understanding of aging as a natural phenomenon. It is attempting to accumulate systematic information concerning behavioral and physiological changes associated with age. In addition, it is systematically investigating age-related impairments of the mental processes in man and is studying possible methods of preventing or repairing such impairments.

This work is being carried out by a staff of psychologists, physiologists, and chemists working under the direction of Dr. James E. Birren.

Most of the deleterious behavioral effects of the aging process that have been demonstrated have been related to motor and reactive capacities. No evidence of degeneration of cortical or subcortical neural materials has as yet been detected. The observed deterioration in problem-solving performance in older subjects appears to be related to a detriment in associative facility and regulation, and much future research will be directed toward discovering ways of compensating for, repairing, or preventing some of the more distressing deficiencies of cognitive functioning associated with age.

The Institute's Laboratory of Clinical Science has been conducting a multidisciplinary investigation, assessing physiological, psychiatric, psychological, and sociological characteristics in a group of elderly symptom-free males. Findings indicate no reductions in cerebral blood flow and oxygen consumption as a result of chronological aging alone but associate such deterioration with arteriosclerosis of the cerebral vessels. In the psychiatric area, it was found that many of the psychiatric conditions are not age determined, but are similar to mental illness of other age groups, indicating that the aged mentally ill need much the same kinds of treatment as younger persons.

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[1] Prepared February 1961 as background information for the Chief of the Division of General Medical Sciences, National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare, in connection with fiscal year 1962 appropriations hearings.

The subjects also cooperated in a sociological investigation. Answers were sought to such questions as: What are the activities, interests, and aspirations that make up day-to-day living? Do earlier patterns of living carry over into old age? How much of behavior is a function of current environmental circumstances? It was determined that there is a relationship between the loss of close relatives and friends and psychiatric assessments of depression and the subject's self-reported decline. Inadequate mental functioning was associated with poor social functioning.

A series of followup studies is planned in which survivors of the group originally studied during 1955–57 will be reevaluated to provide much needed longitudinal data, bearing directly on the course of changes in various psychological functions during the very late years of life.

During the past year, the section on aging completed 11 of the 15 chapters planned for a monograph, to be published in the spring of 1961, which reports the results of the extended, interdisciplinary study of aging.

Members of the staff of the section on aging were called upon during the year to participate in a variety of extramural activities in the United States and abroad. Dr. James E. Birren, chief of the section, conducted a Research Seminar in the Psychological Aspects of Aging and taught a graduate course on the Cognitive Function in Old Age at the University of Chicago. Dr. Birren also presented a paper before the Conference on the Physiology and Psychology of Aging in Paris, France. In addition to these activities, Dr. Birren served as organizer and chairman of the Research Seminar on Psychological Capacities held at Berkeley, Calif. This conference preceded a related conference, the Fifth International Congress of Gerontology, held in San Francisco, at which Dr. Birren acted as program chairman for the section on experimental psychology. Doctors Jack Botwinick and Edward A. Jerome also presented reports on their research at the Fifth International Congress of Gerontology.

At the conclusion of this report (appendix A) is a complete list of professional articles and other written material which were published by the section during 1960.

Gerontology Branch, National Heart Institute

This unit, established in 1941, is under the direction of Dr. Nathan W. Shock and is one of the oldest programs in the field of aging in the United States. The research being done ranges from studies of primitive forms of life to long-term studies on human beings of various age levels. Working with Dr. Shock are histologists, physiologists, biochemists, psychologists, biophysicist, embryologists, zoologists, chemists, and physicians.

The program of the branch is set up under two principal headings: "Basic Biology," including the sections on "Comparative and Cellular Physiology," "Nutritional Biochemistry," "Intermediary Metabolism," "Morphology," "Biophysics," and "Molecular Biology": and "Human Physiology and Clinical Medicine," including the sections on "Cardiovascular-Renal Physiology," "Metabolism and Endocrinology," "Human Performance," "Clinical Medicine," "Psychological Aspects of Aging," "Physiological Psychology," "Mental Performance and Personality."

Studies reported on during 1960 include longitudinal studies made on approximately 250 men age 18 to 100 years, from the upper socio-economic and education levels living in the community. A few preliminary comparisons of measurements made on this selected sample with those made on an indigent population show that some physiological functions show differences, while others do not. For example, the sample group is, on the average, taller and heavier and shows better retention of pulmonary function with increasing age than the indigent group. However, there were no systematic differences in basal metabolism or renal function.

A new equation for estimating body fat in the intact human from determinations of specific gravity or total water content, which introduces corrections for bond density (based on X-ray measurements) and muscle mass (based on creatinine excretion), was developed. Using this equation, a loss of body fat at advanced ages was found.

In another study on 200 subjects, no significant change with age was found in the protein-bound iodine content of the blood.

Age changes in ability to perform simple motions efficiently have been studied using maximum back and forth swings of the arm. Measurements of excess oxygen required for the task have been made which permit the calculation of the efficiency of the motion at different amplitudes and rates of swing. It is apparent that age differences exist in the effectiveness of the mechanism controlling the movement.

Other studies have indicated that age differences in speed of reaction are primarily associated with alterations in the central nervous system.

Short term memory was more easily impaired in old subjects than young. This was true for both visual judgments of areas and estimates of time intervals. In the case of visual judgments, the age-dependent interference was greater in subjects with low educational attainment than in those with high, but for the estimates of time intervals, both groups showed similar degrees of interference.

A mathematical analysis of mortality data has permitted a rational derivation of the Gompertz equation, with the identification of coefficients of the equation that can serve as an index of "vitality" in a population.

With increasing age, granules of insoluble material accumulate inside the cells of cardiac tissue in humans. The granules are highly fluorescent and can be observed microscopically in sections of cardiac tissue. The granules have been isolated from human hearts obtained at autopsy for chemical analysis. Preliminary results indicate that the particles are composed of lipid and protein.

The effects of environmental factors such as temperature, oxygen tension, and radiation on life span have been tested in fruit flies. At increased environmental temperatures longevity is substantially reduced. Exposure to 100 percent oxygen shortens and low oxygen (1–2 percent) lengthens life span in these flies.

These results lend support to the theory that the "rate of living" influences lifespan. High levels of radiation shorten lifespan of flies reared in sterile environments.

Age changes in tissue metabolism are being studied in liver, kidney, brain and muscle of young and senescent rats. Earlier experiments from this laboratory have shown that the activity of a proteolytic enzyme, cathepsin, increases with age.

In other experiments, using radioactive markers, it has been shown that mitochondria probably break down and are resynthesized as units. The half life of liver mitochondria was estimated as 10.3 days in both young and old rats.

Aging has also been studied in protozoan cultures (bleached Euglena) in which cell division has been halted by removing sources of either carbon or nitrogen from the culture medium. Cultures have been maintained at constant cell counts for 3–6 months. The cells remain viable, but the RNA content diminishes markedly with time. When the cells are "aged" in a medium that contains no sulfur they cannot survive for more than about 1 month. Thus the mechanisms which permit the cell to survive in the face of nitrogen or carbon depletion do not function in the case of sulfur depletion.

To carry out this extensive research program the gerontology branch utilizes the facilities of the Baltimore City hospitals which provide for laboratory space; a 50-bed research ward with all facilities for patient care; and access for study to all patients in the 1,500-bed hospital and 1,000-bed Old People's Home.

Preliminary plans for a new Basic Science Research Building, essential to relieve congested laboratory conditions at the Baltimore City hospitals, have been drawn up, with the assistance of members of the staff of the gerontology branch.

At the conclusion of this report (appendix B) is a complete list of articles and other written materials which were published by the branch during the past year.

EXTRAMURAL ACTIVITIES

Center for Aging Research

The Center, established in the fall of 1956, is a branch of the Division of General Medical Sciences. The purpose of the Center is to stimulate and assist the development of new research projects in gerontology at universities, medical centers and various other research institutions in this country and abroad: to maintain liaison between the NIH intramural and extramural program, with other bureaus and divisions of the Department of Health, Education, and Welfare, and with other Federal agencies and organizations supporting programs in aging; to foster the training of additional research personnel; to collect and disseminate data related to research in aging; and to sponsor conferences, symposia, and seminars on research and training problems in the field of aging.

A major activity of the center is the identification of "gap" areas in aging research needing new or additional emphasis. A major basis in determining these "gap" areas is the information obtained through the yearly compilation of the document, "Activities of the NIH in the Field of Gerontology." This publication lists all grants made by NIH for extramural as well as intramural research. The center classifies as relating to aging those projects concerned with changes that reflect time-related processes other than those instrumental in development and growth, and projects concerned with physical, psychological, and social problems of aging people.

The activities of the center during 1960 included giving full cooperation to the White House Conference on Aging, working with the Federal Council on Aging, working with the Federal Aviation Agency with regard to its research grants program in the relationship between aging and pilot performance, assisting and attending many other national and international meetings on aging.

Fourteen major conferences with programs relating to the problems of aging were attended by the staff members during 1960. One of the more notable ones was the Fifth International Congress for Gerontology.

In line with fostering the exchange of information on aging among the countries of the world, the Center for Aging Research is sponsoring the publication of a translation, from the Russian, of the review by Prof. V. N. Nikitin, corresponding member of Ukranian Soviet Socialist Republic Academy of Sciences," Russian Studies on Age-associated Physiology, Biochemistry, and Morphology." This review covers Russian research in aging between 1761 and 1958. The Clinical Center Library translated the text, and the Russian scientific translation program translated the bibliography.

Other informational activities of the center include the preparation and distribution of "Research Highlights in Aging, Summary of NIH Research Programs in Aging," and the "Activities of the NIH in the Field of Gerontology." All booklets are available upon request to the Center for Aging Research.

A list of the speeches given and papers published by members of the CAR staff and other members of the Division of General Medical Sciences appears in appendix D at the conclusion of this report.

Expenditures for extramural research in aging sponsored by NIH have risen from $4,570,000 in 1958 to $16,234,564 in fiscal year 1960. It is anticipated that they will reach $20 million in 1961. Another million dollars is spent annually in the conduct of the intramural research program in aging.

Extramural projects have risen in number from 274 in 1958 to 700 in 1960, with a rise to over 800 anticipated for 1961. The projects listed by the Center for Aging Research represent that portion of the total number of submitted projects which specifically bears upon major problems of aging.

At the conclusion of this section are four tables covering the growth of the grant program in aging, reflecting the activity of each Institute and the Division of General Medical Sciences, since 1958.

Interdisciplinary research centers

In addition to the two previously established multidisciplinary programs at Duke University (1957) and Albert Einstein College of Medicine (1958), two new programs were approved and put into operation during calendar year 1960. These were Western Reserve University, Cleveland, Ohio, inaugurated May 1960; and the University of Miami School of Medicine, Coral Gables, Fla., inaugurated September 1960.

The program at Western Reserve University involves the entire university and several affiliated hospitals. Principal attention is being given to the chronic diseases, with emphasis on the rehabilitation aspects. Investigations into the basic biological changes in aging are also being carried out.

At the University of Miami School of Medicine the program will be entirely basic in its approach to aging. It involves the medical school, the main university, and the marine biology laboratory in related studies in anatomy, physiology, biochemistry, microbiology, and botany.

The program established at Duke University in 1957 has been most fruitful. Each year the number of research reports being presented by the Duke scientists is increasing. Some of the papers presented during 1960 are listed in appendix C.

The Duke program emphasizes the psychiatric, psychologic, and social sciences, but also includes biochemical studies and studies on atherosclerosis.

The program at Albert Einstein College of Medicine is focusing on metabolic changes which result with aging, including research in the biochemical, physiological, and pathological alterations. Heart disease is receiving much attention, in addition to those genetic conditions which seem to predispose certain persons to illness.

Papers published by the scientists working at the Albert Einstein College of Medicine are listed in appendix C.

RESEARCH UNITS

The Center for Aging Research and its consultants believe that more universitywide centers should be established, though in most cases not of the magnitude of those now in existence. These plans call for the organization and long-term support of smaller research units in a number of institutions throughout the country. The objectives of such research units would be to provide a stable organization, an atmosphere of common purpose, and an intellectual and scientific environment for integration and concentration of effort focused on studies in aging.

Stimulation of research in the various departments of the institutions would be a major function of these units. Periodic institutionwide seminars on the various aspects of aging would be conducted. Training opportunities would be developed and teaching activities would be fostered.

Division of General Medical Sciences

In its responsibility for supporting research and research training in the sciences basic to medicine and biology, and in public and environmental health and medical care, the Division of General Medical Sciences is carrying out a program primarily aimed at developing more information on the basic biological nature of the aging process in the cells and tissues of the body, in organs such as the liver, and as related to enzymes and hormones. The work includes investigations into the importance of genetics in the character of the aging process and in longevity. Studies on the influences of nutrition and on the effects of man's living and working environments also are being supported, along with investigation into better rehabilitation techniques for older persons. At present the division is supporting a total of 102 projects related to aging.

The Fifth International Congress of Gerontology held August 7–12, 1960, in San Francisco, was sponsored jointly by the Division of General Medical Sciences and the National Heart Institute. More than 1,100 persons representing 35 nations attended this meeting.

National Heart Institute

Effects of aging on human performance are intimately associated with effects of aging on the cardiovascular system since the activity of every organ in the body depends on an adequate supply of blood. The National Heart Institute, realizing that aging brings about major changes in the heart muscle and in blood vessels, pioneered in the conduct and support of gerontological research and continues to develop and sponsor programs of four types: Integrated multidisciplinary projects; research in problems of aging; research in the care of the aged; and programs to train personnel and disseminate gerontologic information.

Gerontologic research conducted by the Institute constitutes one of the most comprehensive and longest established programs of scientific investigation into aging. This growing research activity provides a background of gerontologic knowledge and productive research studies that make it a national and international resource in the field.

Supporting aging research, 70 research and training projects classified as primarily concerned with aging are being currently supported by the National Heart Institute. Projects range from basic research on aging in short-lived lower organisms to integrated, cooperative studies of elderly persons. Scientists are investigating the influence on the aging process of diet, heredity, changes in hormone production, and changes in connection tissue, as well as the mechanisms of cardiac failure in persons over 65 years and the rehabilitation of elderly cardiovascular patients.

As previously reported in the section on the activities of the Division of General Medical Sciences above, the National Heart Institute shared in sponsoring the Fifth International Congress of Gerontology.

The National Heart Institute, working with the Atomic Energy Commission and the American Institute of Biological Sciences, continues to support research conferences on the relationship between radiation and aging.

Three books have been published by an interuniversity committee, which was supported in part by the National Heart Institute. The first book, "Handbook of Aging and the Individual," was edited by Dr. James E. Birren; the second, "Handbook of Social Gerontology," was edited by Mr. Clark Tibbitts; and the third, "Aging in Western Societies," was edited by Dr. Ernest W. Burgess.

National Cancer Institute

Although the true relationship between cancer and the aging process is not known, there is reason to believe that the two may be closely connected. Scientists whose work is supported by grants from the National Cancer Institute are contributing information that could significantly increase knowledge of both malignant disease and the phenomena of aging.

For example, it is generally accepted that our environment contains agents that probably contribute to the development of malignant disease. The fact that older persons have been exposed to such agents for relatively long periods may account for the greater occurrence of cancer in later life. Yet, it is also recognized that not all persons similarly exposed to environmental carcinogens develop malignant disease. Research in the area of environmental cancer will probably shed light on many important aspects of the aging process, including bodily changes that influence liability to malignant disease.

In other studies, scientists have observed that some mammalian cells growing in the test tube ultimately acquire malignant properties. Investigations in this area, which are concerned with the innermost workings of living matter, could provide vital basic knowledge of metabolic processes that are at the heart of the mechanism of aging, the cancer problem, and perhaps all biological phenomena.

National Institute of Arthritis and Metabolic Diseases

This Institute is supporting a number of studies which are attempting to determine the interplay between age of the host and his susceptibility to infection. At the present time seven extramural studies are concerned primarily with problems in the field of aging.

National Institute of Arthritis and Metabolic Diseases

A considerable variety of studies on structural aspects and on physiological and biochemical aspects of aging are supported through research project grants by this Institute. Biophysical techniques, including electron microscopy and X-ray, are being used to delineate the fine molecular and tissue structure of senescent tissues, particularly in bones, joints and endocrine glands. Investigations are also being made of alterations in thyroid and adrenal steroid function and of body composition in aging, of mineral metabolism in bone diseases afflicting the elderly, and of amino acid, vitamin, and other nutritional requirements in relation to aging. Many fundamental studies performed by Institute grantees will provide information on growth, maturation, and degeneration in both single cells and whole organ systems. These include study of factors affecting the lifespan of red blood cells and of formation and deterioration of collagen, the chief constituent of articular cartilage and connective tissue.

Other Institute-supported studies are concerned with many aspects of diseases associated with aging, notably osteoarthritis and osteoporosis. Institute scientists at Bethesda are also investigating osteoporosis, osteoarthritis, processes of collagen formation and aspects of nutrition related to aging.

The Institute participates in the support of a comprehensive program of research in aging at the Yeshiva University's Albert Einstein College of Medicine.

National Institute of Dental Research

With an increasing population of middle-aged and older citizens, periodontal disease has moved to the forefront as a leading cause of tooth loss in this country. This is reflected in epidemiological studies by the Institute to determine the prevalence and severity of oral diseases.

Laboratory experiments have shown that tartar formation, a factor in periodontal disease, is not dependent on the presence of bacteria. Thus, broad biochemical studies now being supported may provide the research leads necessary for an understanding of tartar formation and accompanying tissue changes.

Other basic studies seek to determine the extent to which bacterial endotoxins contribute to the degradation of oral soft tissues. Of particular interest are studies of bacterial enzymes that apparently play a role in the destruction of connective tissue necessary for the support and retention of teeth.

National Institute of Mental Health

Among those social problem areas which are of special concern to the National Institute of Mental Health, the subject of aging involves the greatest number of people. With the increasing complexity of society, the process of aging has become fraught with many mental health problems. The National Institute of Mental Health initiates, coordinates, and supports an extensive research grants program in the field of aging in an attempt to provide fuller understanding of the processes involved, to help alleviate the psychological problems of older people, and to restore to society some of the human potential now lost. The research projects on aging which the Institute supports bridge many disciplines and a wide variety of research approaches. Some of the biologically oriented studies are concentrated on the effect of aging on the central nervous system, senile degeneration of the brain, and cerebral physiology in functional disorders. Other studies of the aging process relate to psychological criteria of aging, attitudes of older people toward death, general social attitudes toward old people, and environmental and personality factors influencing adjustment of older people, including a scientific investigation of adverse consequences of social isolation. Two large multidisciplinary research projects are concerned with the general aspects of the total aging process—physiological, psychological, and social. Another major study is concentrated on aspects of normal aging of older people living in an average community. During 1960 the Institute also supported a special research seminar on the social and psychological aspects of aging in order to promote wider exchange and utilization of new concepts in this field. However, despite research advances, and no matter what the hopes are for prevention of some of the adverse concomitants of old age, geriatric mental problems will continue to be a part of 20th century society. The Institute therefore is also supporting studies aimed at improving methods for care and treatment of psychiatric geriatric patients.

National Institute of Neurological Diseases and Blindness

Seventy-one extramural and several intramural projects are supported by this Institute which relate directly to aging. Of prime interest are studies on changes in nerve cells and tissue function with age, particularly reflex action, cataracts, glaucoma, deafness, and strokes.

These studies have a special bearing on problems of aging and the state of being aged, since the nerve tissues and sensory structure of higher organisms play a controlling role in determining activity.

EXTRAMURAL STATISTICAL SUMMARIES

The following tables show the number and annual value of research and training grants in aging that were active on January 31, 1961, January 31, 1960, January 31, 1959, and January 31, 1958. The fiscal year columns indicate the appropriation from which funds were derived to support these projects. These tables essentially reflect calendar year activity. The date of January 31 was chosen in order to include the actions of the November meetings of the national advisory councils.

NIH research and training grants in aging active as of Jan. 31, 1961

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1959	Fiscal year 1960	Fiscal year 1961	Total
General [1]	36	$83, 288	$411, 525	$912, 662	$1, 407, 475
NCI	14	----------	77, 951	155, 318	233, 269
NHI	70	12, 282	277, 087	1, 363, 169	1, 652, 538
NIAID	7	----------	12, 217	45, 446	57, 663
NIAMD	47	14, 220	169, 665	605, 382	789, 267
NIDR	12	----------	44, 861	145, 250	190, 111
NIMH	31	83, 038	420, 483	479, 662	983, 183
NINDB	28	----------	111, 699	315, 451	427, 150
Total	245	192, 828	1, 525, 488	4, 022, 340	5, 740, 656

SECONDARILY RELATED TO AGING

General [1]	66	$17, 879	$713, 503	$1, 363, 558	$2, 094, 940
NCI	47	----------	384, 588	510, 335	894, 923
NHI	149	94, 410	1, 166, 600	2, 457, 291	3, 718, 301
NIAID	32	9, 878	68, 459	294, 035	372, 422
NIAMD	70	----------	192, 140	1, 173, 791	1, 365, 931
NIDR	24	----------	133, 637	256, 626	390, 263
NIMH	24	----------	309, 278	388, 808	698, 086
NINDB	43	----------	156, 319	802, 723	959, 042
Total	455	122, 167	3, 124, 524	7, 247, 217	10, 493, 908

[1] Division of General Medical Sciences.

NIH research and training grants in aging active as of Jan. 31, 1960

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Fiscal year 1960	Total
General [1]	28		$393, 851	$715, 276	$1, 109, 127
NCI	19		82, 449	279, 697	362, 146
NHI	72		316. 365	1, 400, 322	1, 716, 687
NIAID	4		11, 215	18, 363	29, 578
NIAMD	42		66, 659	567, 432	634, 091
NIDR	19	$14, 384	119, 919	88, 502	222, 805
NIMH	31	72, 678	485, 141	461, 129	1, 018, 948
NINDB	29		131, 018	336, 498	467, 516
Total	244	87, 062	1, 606, 617	3, 867, 219	5, 560, 898

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Fiscal year 1960	Total
General [1]	40		$171, 519	$523, 515	$695, 034
NCI	38		211, 577	469, 738	681, 315
NHI	117		907, 711	1, 792, 053	2, 699, 764
NIAID	21	$18, 384	42, 811	192, 825	254, 020
NIAMD	49	11, 129	104. 670	888, 129	1, 003, 928
NIDR	24	8, 012	156, 697	316, 609	481, 318
NIMH	20		190, 189	228, 416	418, 605
NINDB	29		138, 977	509, 509	648, 486
Total	338	37, 525	1, 924, 151	4, 920, 794	6, 882, 470

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[1] Division of General Medical Sciences.

NIH research and training grants in aging active as of Jan. 31, 1959

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Total
General [1]	15	$18, 192	$532, 231	$550, 423
NCI	20	120, 021	424, 407	544, 428
NHI	60	227, 888	1, 034, 709	1, 262, 597
NIAID	3	20, 350	10, 010	30, 360
NIAMD	35	37. 148	453. 958	491, 106
NIDR	11	38, 785	60, 774	99, 559
NIMH	32	340, 344	514, 716	855, 060
NINDB	21	109, 706	190, 741	300, 447
Total	197	912, 434	3, 221, 546	4, 133, 980

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1958	Fiscal year 1959	Total
General [1]	14	$32, 000	$268, 910	$300, 910
NCI	31	180, 556	263, 353	443. 909
NHI	84	441, 079	1, 192, 186	1, 633, 265
NIAID	10	24, 833	81, 558	106, 391
NIAMD	32	50, 344	528, 042	578, 386
NIDR	19	148, 867	152. 760	301, 627
NIMH	6	43, 499	53, 397	96, 896
NINDB	11	17, 239	144, 508	161, 747
Total	207	938, 417	2, 684, 714	3, 623, 131

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[1] Division of General Medical Sciences.

NIH research and training grants in aging active as of Jan. 31, 1958

PRIMARILY RELATED TO AGING

Institute	Number	Fiscal year 1955	Fiscal year 1957	Fiscal year 1958	Total
General[1]	9		$12,258	$249,419	$261,677
NCI	11		40,853	99,991	140,844
NHI	48		138,700	747,329	886,029
NIAID	None				
NIAMD	14		41,179	132,434	173,613
NIDR	7		29,821	30,122	59,943
NIMH	28	$23,686	162,972	440,641	627,299
NINDB	14		37,751	79,215	116,966
Total	131	23,686	463,534	1,779,151	2,266,371

SECONDARILY RELATED TO AGING

Institute	Number	Fiscal year 1955	Fiscal year 1957	Fiscal year 1958	Total
General[1]	5		$122,262	$81,951	$204,213
NCI	20		90,207	141,437	231,644
NHI	60		349,597	703,682	1,053,279
NIAID	7		2,501	60,574	63,075
NIAMD	21		32,181	192,470	274,651
NIDR	16		121,426	143,872	265,298
NIMH	6		38,298	35,706	74,004
NINDB	8		34,085	83,804	117,889
Total	143		840,557	1,443,496	2,284,053

[1] Division of Research Grants.

Appendix A

Section on Aging, National Institute of Mental Health

PUBLICATIONS AND PAPERS PRESENTED

1. Botwinick, Jack, Robbin, Joseph S., and Brinley, Joseph F., "Age Differences in Card-Sorting Performance in Relation to Task Difficulty, Task Set, and Practice," Journal of Experimental Psychology, volume 59, No. 1, January 1960.

2. Botwinick, Jack and Kornetsky, Conan, "Age Differences in the Acquisition and Extinction of the GSR," Journal of Gerontology, volume 15, No. 1, January 1960.

3. Birren, James E., "Psychological Capacities and the Process of Aging in the Nervous System, A Counterpart Theory of Aging," (1) Presentation at the Conference on the Physiology and Psychology of Aging at the Centre National de la Recherche Scientifique, Paris, France, April 1960. (2) Section on Aging, Laboratory of Psychology.

4. Dallenbach, Karl M., Bitterman, M. E., Newman, E. B. and Postman, Leo, "Basis for Lightness-Judgments of Grays," The American Journal of Psychology, volume LXXIII, pages 380–387, September 1960.

5. Birren, James E., "Psychological Aspects of Aging," Annual Review of Psychology, volume 11, 1960.

6. Birren, James E., "Behavioral Theories of Aging," American Association for the Advancement of Science, 1960.

7. Streicher, Eugene, "The Thiocyanate Space of Rat Brain in Experimental Cerebral Edema."

8. Birren, James E., Butler, Robert N., Greenhouse, Samuel, Sokoloff, Louis, and Yarrow, Marian R., "Introduction to the Study of Human Aging," Birren, J. E. (editor), "Handbook of Aging and the Individual: Psychological and Biological Aspects."

9. Streicher, Eugene, "The Thiocyanate Space of Rat Brain."

10. Bondareff, William, "Distribution of Nissl Substance in Neurons of Rat Spinal Ganglia as a Function of Age and Fatigue."

11. Jerome, Edward A., "Decay of Heuristic Processes in the Aged."
12. Jerome, Edward A., "Thinking Ability in the Aged."
13. Birren, James E., "Part I: Intellectual Capacities, Aging and the Nature of Man's Environment—A Discussion of Issues and a Report of Experimental Findings." Part II, Birren, James E., and Morrison, Donald F., "Factors in the Organization of Mental Abilities with Advancing Age: Analysis of Intercorrelations of the Wais Subtests in Relation to Age and Education." Part III, Birren, James E., and Riegel, Klaus F., "Age Differences in Response Speed as a Function of Controlled Variations of Stimulus Conditions: Lights, Numbers, Letters, Colors, Syllables, Words, and Work Relationships."
14. Birren, James E., Botwinick, Jack, Weiss, Alfred D., and Morrison, Donald F., "Cognitive Processes: III—An Analysis of Mental and Perceptual Tests Given to Healthy Elderly Men."

Appendix B

Gerontology Branch, National Heart Institute

PUBLICATIONS AND PAPERS PRESENTED

1. Shock, Nathan W., "Index to Current Periodical Literature," Journal of Gerontology, volume 15, No. 1, January 1960.
2. Blum, Jacob J., "Interaction Between Myosin and its Substrates," Archives of Biochemistry and Biophysics, volume 87, No. 1, March 1960.
3. Searls, R. L. (introduction by Zill, L. P.), "Evidence for Dithiol Participation in Dihydrothioctyl Dehydrogenase Reaction," Federation Proceedings, volume 19, No. 1, part I, March 1960.
4. Fluharty, A. L., and Sanadi, D. R., "Evidence for Dithiol Function in Oxidative Phosphorylation Based on Uncoupling by Arsenite," Federation Proceedings, volume 19, No. 1, part I, March 1960.
5. Baker, Saul P., Shock, Nathan W., and Norris, Arthur H., "Effects of Age and Obesity on Basal Oxygen Consumption of Women as Related to Body Fluid Compartments," Federation Proceedings, volume 19, No. 1, part I, March 1960.
6. Mildvan, A. S., and Strehler, B. L., "Fluorescent Lipids From Heart Age Pigment," Federation Proceedings, volume 19, No. 1, part I, March 1960.
7. Ramsey, Robert W., Norris, A. H., LeVora, N. W., Shock, N. W., Street, Sybil, Bower, John, Miller, M. R., Rudolph, Rosser and Szumski Alfred, "An Analysis of Alternating Movements of the Human Arm," Federation Proceedings, volume 19, No. 1, part I, March 1960.
8. Searls, Robert L., and Sanadi, D. R., "Evidence for a Vicinal Dithiol in Dihydrothioctyl Dehydrogenase," Biochemical and Biophysical Research Communications, volume 2, No. 3, March 1960.
9. Searls, Robert L., and Sanadi, D. R., "Oxidation of -Ketoglutarate by Artificial Electron Acceptors," Biochemical and Biophysical Research Communications, volume 2, No. 3, March 1960.
10. Norris, A. H., and Shock, N. W., "The Six S's," Newsletter of the Gerontological Society, volume 7, No. 1, March 1960.
11. Shock, Nathan W., "Index to Current Periodical Literature," Journal of Gerontology, volume 15, No. 2, April 1960.
12. Barrows, Charles H., Jr., Falzone, Joseph A., Jr., and Shock, Nathan W., "Age Differences in the Succinoxidase Activity of Homogenates and Mitochondria From the Livers and Kidneys of Rats," Journal of Gerontology, volume 15, No. 2, April 1960.
13. Fluharty, Arvan, and Sanadi, D. R., "Evidence for a Vicinal Dithiol in Oxidative Phosphorylation," Proceedings of the National Academy of Sciences, volume 46, No. 5, pages 608–616, May 1960.
14. Blum, Jacob J., "Concentration Profiles in and Around Capillaries," The American Journal of Physiology, volume 198, No. 5, May 1960.
15. Baker, Saul P., Landowne, Milton, and Gaffney, George W., "Electrocardiographic Changes Following the Administration of Thyroid Stimulating Hormone," the American Journal of Cardiology, volume 5, page 707, May 1960 (abstract).

16. Searls, Robert L., and Sanadi, D.R., "On the Mechanism of Dihydrothioctyl Dehydrogenase Reaction," the Journal of Biological Chemistry, volume 235, No. 8, June 1960.

17. Strehler, Bernard L., and Mildvan, Albert S., "General Theory of Mortality and Aging," Science, volume 132, No. 3418, pages 14–21, July 1960.

18. Gaffney, George W., Gregerman, Robert I., Yiengst, Marvin J., and Shock, Nathan W., "Serum Protein-Bound Iodine Concentration in Blood of Euthyroid Men 18 to 94 Years," Journal of Gerontology, volume 15, No. 3, July 1960.

19. Shock, Nathan W., "Index to Current Periodical Literature," Journal of Gerontology, volume 15, No. 3, July 1960.

20. McCarthy, Joseph D., Shock, Nathan W., Swartz, Frederick C., and Weinberg, Jack, "Panel Discussion on Concepts of the Medical Profession in Relation to Aging," Journal of the American Geriatrics Society, volume VIII, No. 8, August 1960.

21. Searls, Robert L., Sanadi, D. R., "-Ketoglutaric Dehydrogenase, VIII. Isolation and Some Properties of a Flavoprotein Component," the Journal of Biological Chemistry, volume 235, No. 8, August 1960.

22. Konigsberg, Irvin R., "On the Relationship Between Development and Aging," Newsletter of the Gerontological Society, volume 7, No. 3, September 1960.

23. Shock, Nathan W., "Index to Current Periodical Literature," Journal of Gerontology, volume 15, No. 4, October 1960.

24. Hugin, Felix, Norris, Arthur H., and Shock, Nathan W., "Skin Reflex and Voluntary Reaction Times in Young and Old Males," Journal of Gerontology, volume 15, No. 4, October 1960.

25. Barrows, Charles H., Jr., "Age and Cellular Metabolism of Tissues," the Biology of Aging, American Institute of Biological Sciences Symposium, No. 6, 1960.

26. Mildvan, Albert S., and Strehler, Bernard L., "A Critique of Theories of Mortality," the Biology of Aging, American Institute of Biological Sciences Symposium, No. 5, 1960.

27. Suci, George J., "A Comparison of Semantic Structures in American Southwest Culture Groups," Journal of Abnormal and Social Psychology, volume 6z, No. 1, 25–30, 1960.

28. Strehler, B. L., "Fluctuating Energy Demands as Determinants of the Death Process (a Parsimonious Theory of the Gompertz Function)," the Biology of Aging, American Institute of Biological Sciences Symposium, No. 6, 1960.

29. Shock, N. W., "Age Changes in Physiological Functions in the Total Animal: The Role of Tissue Loss," the Biology of Aging, American Institute of Biological Sciences Symposium, No. 6, 1960.

30. "Author Index to Current Periodical Literature," Journal of Gerontology, volume 15, No. 4, October 1960.

APPENDIX C

DUKE UNIVERSITY SCHOOL OF MEDICINE AND ALBERT EINSTEIN COLLEGE OF MEDICINE

PUBLICATIONS AND PAPERS PRESENTED

Duke University

1. Busse, Ewald W., Dovenmuehle, Robert H., and Brown, Robert G., "Psychoneurotic Reactions of the Aged," Geriatrics, volume 15, pages 97–105, February 1960.

2. Busse, Ewald W., "Clinical Principles Underlying Administrative Practices," Mental Hospitals, 11th Mental Hospital Institute Proceedings, "The Geriatric Patient-Psychiatric and Social Problems," volume 11, No. 2, February 1960.

3. Busse, E. W., and Dovenmuehle, R. H., "Neurotic Symptoms and Predisposition in Aging People," Journal of the American Geriatrics Society, volume VIII, No. 5, May 1960.

4. Davidson, Eugene A., and Riley, Joseph G., "Chondroitin Sulphate B Metabolism," Biochimica et Biophysica Acta, June 1960.

5. Busse, Ewald W., "The Health and Adjustment of the Aged Person," address delivered at the Governors' conference on aging, July 28, 1960, Raleigh, N.C.
6. Gunnells, J. C., Gorten, R., Bogdonoff, M.D., and Warren, J. V., "The Effect of Alterations in Arousal of the Central Nervous System Upon Cardiovascular Response to Intravenous Epinephrine," American Heart Journal, volume 60, No. 2, pages 231–236, August 1960.
7. Jeffers, Frances, Nichols, Claude R., and Eisdorfer, Carl, "Attitudes of Older Persons Toward Death: A Preliminary Study." A version of this paper was delivered at the Fifth Congress of the International Association of Gerontology, San Francisco, Calif., August 1960.
8. Busse, Ewald W., "Findings from the Duke Geriatrics Research Project on the Effects of Aging Upon the Nervous System." Presented at the Fifth International Congress of Gerontology, San Francisco, Calif., August 1960; submitted for publication in the proceedings of this congress.
9. Busse, Ewald, W., "The Health and Adjustment of the Aged Person," Public Welfare News, 24 : 3, September 1960.
10. Wakil, Salih J., "The Mechanism of Fatty Acid Synthesis," American Journal of Clinical Nutrition, volume 8, September–October 1960.
11. Busse, Ewald W., "Problems Affecting Psychiatric Care of the Aging," Geriatrics, volume 15, pages 673–680, October 1960.
12. Dovenmuehle, R. H., Newman, E. G., and Busse, E. W., "Physical Problems of Psychiatrically Hospitalized Elderly Persons," Journal of the American Geriatrics Society, volume VIII, No. 11, November 1960.
13. Newman, Gustave, Dovenmuehle, R. H., and Busse, E. W., "Alterations in Neurologic Status With Age," Journal of the American Geriatrics Society, volume VIII, No. 12, December 1960.
14. Klein, Robert F., and Bogdonoff, Morton D., "Effects of Phentolamine (Regitine) on Human Plasma FFA in vivo (25590)," Proceedings of the Society for Experimental Biology and Medicine, 1960.
15. Busse, Ewald W., "Mental Disorders of the Aging," the Older Patient, by 21 authors, edited by Wingate M. Johnson, M.D.; publishers, Paul B. Hoeber, Inc., Medical Division of Harper & Bros., 1960.

IN PRESS

1. Jeffers, Frances C., "The Nature and Significance of Social Work Participation in Interdisciplinary Research on Aging," accepted for publication in Geriatrics.

Albert Einstein College of Medicine

PUBLICATIONS AND PAPERS PRESENTED

1. Lippmann, Heinz I., and Goldin, Ralph R., "Subcutaneous Ossification of the Legis in Chronic Venous Insufficiency," Radiology, volume 74, No. 2, pages 279–288, February 1960.
2. William, M. Henry, Jr., and Zohman, Lenore R., "Cardiopulmonary Function in Bronchial Asthma," the American Review of Respiratory Diseases, volume 81, No. 2, February 1960.
3. London, Irving M., "Metabolism of the Mammalian Erythrocyte," Bulletin of the New York Academy of Medicine, second series, volume 36, No. 2, pages 79–96, February 1960.
4. Cook, Jean L., Lowy, Bertram A., and London, Irving M., "Purine Necleotide Biosylnthesis in the Rabbit Reticulocyte," Federation Proceedings, volume 19, No. 1, part I, March 1960.
5. Williams, M. Henry, Jr., "Hypoxemia Due to Venous Admixture in Cirrohis of the Liver," Journal of Applied Physiology, volume 15, No. 2, March 1960.
6. Morrell, Anatol G, and Scheinberg, I. Herbert, "Heterogeneity of Human Ceruloplasmin," Science, volume 131, No. 3404, pages 930–932, March 1960.
7. Weinstein, Clement, Seifter, S., and Berkman, J. E., "Peptide-Nucleotide Associations in Rat Liver," Federation Proceedings, volume 19, No. 1, part I, March 1960.
8. Aisen, Philip, Schorr, Julian B., Morell, Anatol G., Gold, Ruth Z. and Schienberg, I. Herbert, "A Rapid Screening Test for Deficiency of Plasma Ceruloplasmin and Its Value in the Diagnosis of Wilson's Disease," the American Journal of Medicine, volume XXVIII, No. 4, pages 550–554, April 1960.

9. Scheinberg, I Herbert and Sternlieb, Irmin, "The Pathogenesis and Clinical Significance of the Liver Disease in Hepatolenticular Degeneration (Wilson's Disease)," the Medical Clinics of North America, volume 44, No. 3, May 1960.

10. Arias, Irwin M., "Recent Advances in the Metabolism of Bilirubin and Their Clinical Implications," the Medical Clinics of North America, volume 44, No. 3, May 1960.

11. Abramson, Arthur S., and Delagi, Edward F., "The Contributions of Physical Activity to Rehabilitation," the Research Quarterly, 31: 2, pages 365–375, May 1960.

12. Deming Q. B., Daly, M. M., Bloom, J., Brun, L, Kaplan, R, "Effect of Antihypertensive Treatment in the Rat on the Potentiation of Artherogenesis by Experimental Hypertension," Journal of Clinical Investigation, volume 39, No. 6, page 980, June 1960.

13. Lippmann, Heinz, "Heteroptic Ossification, A Problem in Rehabilitation Medicine," Archives of Physical Medicine and Rehabilitation, volume 41, August 1960.

14. Scheinberg, I. Herbert, and Sternlieb, Irmin, "The Long-Term Management of Hepatolenticular Degeneration (Wilson's Disease)," the American Journal of Medicine, volume XXIX, No. 2, pages 316–333, August 1960.

15. Scheinberg, I. Herbert, and Sternlieb, Irmin, "Copper Metabolism," Pharmacological Reviews, volume 12, No. 3, September 1960.

16. Gallop, Paul M., Seifter, Sam, Lukin, Marvin, and Meilman, Edward, "Application of the Lossen Rearrangement of Dinitrophenylhydroxamates to Analysis of Carboxyl Groups in Model Compounds and Gelatin," the Journal of Biological Chemistry, volume 235, No. 9, September 1960.

17. Seifter, Sam, Gallop, Paul M., Michaels, Susan, and Meilman, Edward, "Analysis of Hydroxamic Acids and Hydrazides; Preparation and Properties of Dinitrophenyl Derivatives of Hydroxamic Acids, Oximes, Hydrazides, and Hydrazones," the Journal of Biological Chemistry, volume 235, No. 9, September 1960.

18. Makover, H. B., "Demography in the Medical Curriculum," Journal of Medical Education, 35: 809–811, September 1960.

19. Fischel, Edward E., and Frank, Charles W., "The Evolution of Rheumatic Heart Disease in Children, 5-Year Report of a Cooperative Clinical Trial of ACTH, Cortisone, and Aspirin," Circulation, volume XXII, No. 4, October 1960.

20. Lowy, Bertram A., Ramot, Bracha, and London, Irving M., "The Biosynthesis of Adenosine Triphosphate and Guanosine Triphosphate in the Rabbit, Erythrocyte in Vivo and in Vitro," the Journal of Biological Chemistry, volume 235, No. 10, October 1960.

21. Lowy, Bertram A., and Williams, Marjorie K., "The Presence of a Limited Portion of the Pathway de Novo of Purine Nucleotide Biosynthesis in the Rabbit, Erythrocyte in Vitro," the Journal of Biological Chemistry, October 1960.

22. Weinstein, S., "Tactual Sensitivity as a Function of Handedness and Laterality," Journal of Comparative and Physiological Psychology, November 1960.

23. Delagi, Edward F., "Rehabilitation of the Homebound in a Semirural Area," Journal of Chronic Diseases, 12: 5, November 1960.

24. von Hippel, Peter H., Gallop, Paul M., Seifter, Sam, and Cunningham, Robert S., "An Enzymatic Examination of the Structure of the Collagen Macromolecule," Journal of the American Chemical Society, 1960.

25. White, Abraham, "Some Biochemical Aspects of Aging," American Association for the Advancement of Science, Aging, 1960.

26. Arias, Irwin, M., "The Chemical Basis of Kernicterus," Advances in Clinical Chemistry, volume 3, 1960.

27. Williams, M. H., Jr., "The Effect of Voluntary Increase of the Tidal Volume on the Steady-State Diffusing Capacity of the Lung," Clinical Research, 8: 381 (abstract), 1960.

28. Williams, M. H., Jr., book, "Clinical Applications of Cardiopulmonary Physiology," Paul B. Hoeber, Inc., 1960.

29. Gidez, L. I., Sorensen, D. K., Shreeve, W. W., and Eder, H. A., "Synthesis of Cholesterol (in vivo) from (2–C^{14}), Mevalonic Acid in Humans and Swine" (abstract), Biochemistry of Lipids, edited by G. Popjak, Pergamon Press, London, 1960.

30. Gilon, E., Roheim, P. A., and Eder, H. A., "The Effect of Phentolamine on Serum Free Fatty Acids in a Patient With a Pheochromocytoma and in Normal Subjects" (abstract), Circulation, 21 : 679, 1960.
31. Roheim, P. A. Haft, D. E. White, A., and Eder, H. A., "In Vitro, Exchange of Cholesterol in Lipoprotein Fractions" (abstract), Circulation, 21 : 652, 1960.
32. Frank, C. W., "Spatial Separation of Sequential Portions of the Inspirate in the Normal Lung," the Physiologist, 3 : 59, 1960.
33. Frank, C. W., Kiefhaber, F. H., Jordan, A., Akyol, T., Galton, B., and Arora, Y., "Assessment of Mitral Regurgitation by Dye Dilution Technics," Clinical Research, 1960.
34. Makover, H. B., "Public Health Problems of Juvenile Delinquency," editor and participant, Academy of Pediatrics, Journal of Pediatrics, spring 1960.
35. Makover, H. B., "Report of Proceedings of Little White House Conference on Aging," monograph, 1960.
36. Laragh, J. H., Ulick, S., Vlodzimerz, J., Deming, Q. B., Kelly, W. G., Lieberman, S., "Aldosterone Secretion and Primary and Malignant Hypertension," Journal of Clinical Investigation, volume 39, No. 7, page 1091, 1960.

IN PRESS

1. Abramson, A. S., Delagi, E. F., "The Influence of Weight-Bearing and Muscle Contraction on Disuse Osteoporosis," (*a*) Proceedings Third International Congress of Physical Medicine, (*b*) Archives of Physical Medicine.
2. Abramson, A. S., and Delagi, E. F., "Critical Factors in Electromyographis Instrumentation," Archives of Physical Medicine and Rehabilitation.
3. Jaffe, E. R., and Gordon, E. D., "Incorporation of Nicotinic Acid Into Pyridine Nucleotides of Erythrocytes and Reticulocytes of Rabbits," Federation Proceedings.
4. Makover, H. B., "Communications in Public Health," delivered at Eastern States Health Conference, May 1960.
5. Makover, H. B., "Statistical Reasoning," Journal of Indian Medicine Profession, Bombay, India.

APPENDIX D

CENTER FOR AGING RESEARCH

PUBLICATIONS AND PAPERS PRESENTED

1. Hunt, G. Halsey, Frame, Elizabeth, and Mohler, Stanley R., "Annual Administrative Review : Chronic Illness," Journal of American Hospital Association, April 1960.
2. Mohler, Stanley R., "Problems of Gerontology in the United States," Pan American Medical Association (copies available), May 1960.
3. Mohler, Stanley R., "Aging and Pilot Performance, Current Related Research and Research Needs," postgraduate course in aviation medicine, Ohio University (copies available) September 1960.
4. Gerber, Joseph H., "Current Gerontological Research," Fourth Annual New England Conference on Aging (no text available), October 1960.
5. Gerber, Joseph H., "Nutritional Aspects of Medical Research for the Aging," American Dietetics Association (no text available), October 1960.
6. Hunt, G. Halsey, "Recent Advance in Geriatrics," Public Health Reports, December 1960.
7. Mohler, Stanley R., "Aspects of Gerontology in the United States," Public Health Reports, December 1960.

ALCOHOLISM

Dr. FELIX. You asked me about alcoholism.

Mr. FOGARTY. We instructed you 3 years ago to start doing more work in this field and gave you $750,000 over the budget to start doing some special research.

Dr. FELIX. I think it was 3 years ago.

Mr. FOGARTY. What is your budget for 1962 in this area of alcoholism?

Dr. FELIX. I don't have a projection for 1962. I can give you the figure for 1960 and for 1961. The exact figure for 1960 was $1,569,000. In 1961 it will be just about $1,900,000 in alcoholism. There are a number of very interesting programs going on here.

Mr. FOGARTY. This is still a very serious problem, isn't it?

Dr. FELIX. Yes, sir, it is.

Mr. FOGARTY. Is it more serious in men or women?

Dr. FELIX. Numberwise, there are more men than women. As to its seriousness, it looks as though in many cases it is more devastating in women than in men, probably because of the type of responsibilities women have for home, children, and so forth—not that the husbands don't have responsibilities, too; but they are much more closely identified with the women.

It is a serious problem both ways. I also have a report in this area that I can submit, if you would like, sir.

Mr. FOGARTY. We will place it in the record.

(The report requested follows:)

ALCOHOLISM

INTRODUCTION

The field of alcoholism continues to be an important concern of the National Institute of Mental Health. The Institute's program in this field is designed to stimulate research, to raise the level of scientific inquiry, to aid in clarifying the uncertain knowledge which currently exists, to improve diagnostic and therapeutic techniques, and to provide consultation services to the States and other professional and lay groups interested in the problem.

Alcoholism is viewed by the Institute as a reaction to a series of stressful situations generated by a dynamic and complex interaction of physical, psychological, and social factors. The extent to which each of these factors contributes to the alcoholism syndrome is not now known. While the development of effective treatment and prevention techniques does not necessarily have to await the determination of the specific etiology of alcoholism such determination will aid in reducing its incidence and prevalence. The Institute's program is, therefore, planned to acquire knowledge pertaining to the relationships among the physical, psychological, and social factors.

PROGRAM DEVELOPMENT

Four projects are of major importance in the Institute's program for research in the field of alcoholism. While these projects vary in content and method, the common underlying purpose is to meet a crucial need in the field: to clarify and evaluate existing knowledge. The projects are in various stages of development and no statements about their ultimate results can be made. However, it is likely that they will make important contributions to the understanding of alcoholism.

Cooperative Commission on the Study of Alcoholism

Members of the Institute's staff have been working with the North American Association of Alcoholism Programs (NAAAP) for the past several years in a combined effort to establish a cooperative commission which will have the responsibility for systematically reviewing and organizing the current state of knowledge in the field. Although the Institute and NAAAP have cooperated in the formation of the commission, it will function as an independent entity under a research grant from the Institute.

The major tasks of the cooperative commission, under the direction of a scientific director, are: (1) to make a comprehensive study of such scientific knowledge as now relates to alcohol use and alcoholism; (2) to inventory, study, and evaluate activities, programs, and resources now playing a significant part in attempts to solve or control the problems of alcoholism; (3) to investigate relationships between alcoholism organizations and other resources such as those in the fields of mental health, tuberculosis control, correction, and professional schools for the training of treatment and research personnel; (4) to use the results of these studies to formulate policies and recommendations for improving treatment, education, and prevention, and (5) to identify in broad terms what further research is urgently needed.

Dr. Nevitt Sanford, professor of psychology at the University of California and currently at the Center for Advanced Study in the Behavioral Sciences, Stanford University, has been appointed scientific director of the project. Though preliminary work is underway, the major program awaits the final constitution of the commission and the recruitment of the staff. The project will undertake a complete review and evaluation of the many facets of alcoholism. Several task forces will be formed to investigate specific areas. The scientific director will assume responsibility for the overall direction of the the work which, in turn, will provide material for a major, long-term university study of problems related to the use of alcohol.

Alcohol usage patterns

The purpose of this project is to develop instruments for gathering data about nonpathological alcohol consumption. It is essential that such data be gathered if a baseline from which to measure deviation in drinking patterns is to be established. This project is located in the Division of Alcoholic Rehabilitation of the California State Department of Public Health.

Influence of sociocultural factors

It is known that social factors influence the drinking behavior of individuals; the extent and manner in which they are involved in the development of alcoholism is not known. The third project deals with the values and habits surrounding alcohol usage as they are affected by the cultural factors of various ethnic groups. This study is being conducted in Colorado.

Nomenclature

The fourth project is a nomenclature study. Its purpose is to clarify the confusing state of terminology in the alcoholism field. It will also recommend a nomenclature which can be integrated with the standard classified nomenclature of the AMA–APA and will be useful for research and treatment purposes.

RESEARCH

The investigations being supported by the Institute range from the specific drug effects of the ingestion of alcohol to the analysis of the complex social relationships involved in problem drinking. For example, some studies are concerned with the effects of chemical agents, including alcohol, cerebral oxidation and the manner in which alcohol is metabolized. Others are concentrating on the effects of alcohol on psychological processes. Sociological factors are also being investigated; one study is concerned with the behavior of the wives of alcoholics. Research support is also provided to investigators interested in the treatment and rehabilitation of the alcoholic.

PROFESSIONAL AND TECHNICAL ASSISTANCE

Consultation and technical assistance is provided to the States through the mental health consultants. In addition, technical assistance projects (TAP's) are also available to aid States in their alcoholism programs. These projects provide funds for workshops and conferences held in a specific State on a particular problem and have proven to be an effective mechanism for strengthening State alcoholism programs. Nine technical assistance projects were supported during 1961; last year eight States received such support. The following States have held TAP conferences during the current year: California, Colorado, Vermont, Kansas, Missouri, New Jersey, New Mexico, North Dakota, and Mississippi.

The Institute's Mental Health Study Center continued its collaborative pilot project with the Prince Georges County (Md.) Health Department and is in the second year of a 4-year demonstration on public health approach to problems of alcoholism in the family. The project has three broad purposes—rehabilitation of the alcoholic and his or her family through the combined efforts of appropriate community facilities, development of an educational and preventive program, and evaluation.

Further attention and emphasis was given to alcoholism program activities already in several State departments of public health, some of which are State mental health authorities, and in some State mental health agencies other than State health departments. For example, State health departments in Kansas, South Dakota, and Wyoming, which are also State mental health authorities, make considerable use of technical assistance and consultation. At the same time, State alcoholism commissions and boards made use of similar assistance and consultation. They showed much interest also in developing closer collaboration with State health departments and with other State agencies. Thus, it is encouraging to note that the general trend of State alcoholism programs is to become more closely associated with State public health departments.

OVERVIEW

While progress is being made in the study of alcoholism, certain critical problems remain. These are the problems of the shortage of scientific personnel, the inadequate and inaccurate body of knowledge, and the generally low prestige of alcoholism as a field of study. These are not new problems and they must be solved if progress is to continue.

The Institute is concerned with the individual alcoholic as he functions within a social matrix. Thus, socioenvironmental and psychological factors assume equal importance with the physiological factor. The Institute's program has been developed to tap all three bodies of knowledge.

Table of obligations

Actual, 1960	$1,569,000
Estimate, 1961	1,897,000
Estimate, 1962	2,889,000

Mr. Fogarty. Give us the highlights of what is being done.

COOPERATIVE COMMISSION ON THE STUDY OF ALCOHOLISM

Dr. Felix. You remember several years ago we made a grant in the field of mental retardation to a group to survey the whole field and come up with a report on what was needed, what was presently known, and where we should go next.

Dr. Masland, incidentally, was a member, before he came with the Federal Government, one of the three investigators who prepared that report. On the basis of that, Dr. Masland's institute and ours have gone forward in trying to follow this.

The National Institute of Mental Health started the same thing in the field of alcoholism. We have made a grant to a group which has been created, known as the Cooperative Commission on the Study of Alcoholism, which is really under the aegis of the North American Association of Alcoholism Programs.

This latter group is an organization consisting of the official authority in each State and in the Provinces of Canada responsible for dealing with the problem of alcoholism under the State or Provincial governments in these areas. They have now appointed a very distinguished man as project director. He is now on the job—Dr. Sanford, of the University of California.

They are going to look into three areas. They want to look into the present state of knowledge in the field of alcoholism and evaluate present activities. In other words, things that are going on now. Are they really paying off, or are they not, and how could they be modified in their best judgment?

They also are going to look into the relationships between organizations dedicated primarily to the problem of alcoholism and other organizations and activities to see what coordination there is here, and what more should be done. They will come up with a series of recommendations, policy recommendations, for the guidance of the States, because, while this is not under the control of, it is under the aegis of, the State directors.

They will also do a survey of present research and give recommendations identifying future areas of research which will be carried on. It will be a year or two before this is out, as it was in the case of the retardation program. But I would anticipate the same thing here that did occur there, that this will provide guidelines for the future which will help us a great deal.

ALCOHOL USAGE PATTERNS

We are doing a study—I am going to mention this and I know somebody is going to smile because of the fact that it looks as though perhaps we are getting a little away, but it is not. We are doing a study of normal alcohol usage among normal, nonalcoholic people. How do they drink? When do they drink? How much do they drink? Under what conditions and what is the result?

The reason for this in all seriousness is very good. We have to know what the normal baseline is in any situation before we can study and make any accurate evaluation of pathology. I think I have discussed this with this committee before. We have all kinds of definitions of what is alcoholism.

One person may say, and you have heard it said, that anyone who takes a drink before noon is either an alcoholic or potentially an alcoholic. But is this so? Others will say that anyone who regularly takes a drink, takes a cocktail every evening before dinner, is either potentially an alcoholic or is an alcoholic; that unless you break this up so it becomes irregular and not routine, this becomes pathology.

Is this so? Well, if you use a normative approach, if the majority of people who use alcohol and are functioning adequately drink, say, a cocktail every evening, this is a baseline from which we can depart.

Then there comes a question as to how many drinks a day makes an alcoholic. Again we wish to study this.

CULTURAL STUDIES

We are also conducting a study of alcohol usage in one part of the country where three different cultures come together and live more or less together, to find out what the ethnic differences are in drinking patterns.

In this area there are native American Caucasians; there are American Indians; and there are Spanish Americans who have migrated from across the border. We are studying the drinking patterns in these three groups and relating that to a whole variety of factors, including status level, occupation, income level, and so forth.

We also have a project going to reassess and redefine the nomenclature in the field of alcoholism. This is not only for the purpose of making understandable one person's research when you compare it with another one in this country, but to bring this in line with the international classification, because we also want to do some studies in this area as quickly as we can, comparative studies with other countries—Scandinavian countries, some of the other Anglo-Saxon countries, and some other places.

The reasons for this are several. Drinking patterns vary from country to country. Some countries are primarily brew drinkers—that is, beer drinkers. Some are drinkers of ferments such as wines: and others are drinkers of hard liquor.

It also appears that in some of these countries where traditionally they have been, let's say, brew drinkers, the younger generation is shifting to a hard liquor or a distilled brew type of drinking. What does this mean, if anything? We have to get some solid information first before we can do this.

Mr. Fogarty. Are you getting information in countries like India?

Dr. Felix. We would hope to get some information on countries such as that. We also have another angle here. There are certain classes or ethnic groups of people in this country and elsewhere who use alcohol routinely in one form or another as a ritual. I don't mean just a sip or intinction of a wafer, but who use it routinely at meals and so forth. In some of these groups we find alcoholism remarkably low.

We would like to know more about why this is. But we have to get our definitions straight before we will be able to do this.

During this past year we have contracted for several technical assistance projects in several States—California, Colorado, Vermont, Kansas, Missouri, New Jersey, New Mexico, North Dakota, and Mississippi. All of these held statewide conferences on alcoholism and its control as related to the problems in their State.

As you know, under these technical assistance projects one of the requirements is that the proceedings, recommendations, and conclusions be published. The National Institute of Mental Health is supplied with enough copies so that each State can be supplied with an adequate number of copies for its guidance.

These have been disseminated now, or will be if they are not all in yet, to every State and territory of the Union.

Mr. Fogarty. Are you working with Alcoholics Anonymous?

Dr. Felix. At the moment, not officially.

Mr. Fogarty. They do some good work; don't they?

Dr. Felix. Yes, they do. They certainly do.

DRUG ADDICTION

Mr. Fogarty. What about drug addiction?

Dr. Felix. In 1961 we will expend approximately $1 million in the field of drug addiction. Our anticipated figure is $990,000 plus, around $1 million. In our own direct operations, much of the research is going on at the Addiction Research Center at Lexington, where they are studying various chemical compounds for addicting properties.

I might say here, before I forget it, they are now testing a new synthetic drug which goes by the code name of I–K–1, which appears to be as effective as codeine for relieving pain in about one-seventh of the dose.

So far—and this is not an official statement, but merely an impression so far—this substance is sufficiently nonaddictive that it may well be that it won't have to come under the Harrison Narcotic Act. We have been working, as you know, 25 years to find a substance of this kind. In other words, a seventh of a grain of this is as effective as a grain of codeine, and it is much, much less addictive.

In the past so frequently we have found substances that could be taken in smaller doses; but the addictive qualities went up proportionately. This new drug has gone in just the other direction. This is a real advance.

We have been carrying on, as you know, for several years in New York City a demonstration project in which we have been following up on addicts from the Lexington Hospital. We have been able to bring into cooperation with us almost all of the agencies in New York, including the police department, the welfare department, and others, to try to give them enough supporting services and followup services so that they would remain free of drugs.

Mr. Fogarty. You can expand on that in the record.

(The following statement was submitted later:)

Drug Addiction

INTRODUCTION

The National Institute of Mental Health is making a broad and diversified attack on the problem of drug addiction, ranging from the biochemical effects of narcotic drugs to efforts of community agencies to prevent relapse of addict patients. The major work on drug addiction in the Institute is being done through programs of community mental health services, research conducted by Institute staff, and research grants.

COMMUNITY SERVICES PROGRAMS

It has generally been assumed that the lack of community facilities for post-institutional treatment and rehabilitation is one important reason for the relapse of drug addicts who have been released from institutions. Most social welfare agencies and health agencies have been reluctant to accept addicts. The Institute, therefore, established a demonstration center in New York City in 1957. The referral program of the center was undertaken as a pilot operation to determine whether or not community agencies in New York City would extend their services to the drug addict (initially on a limited basis) as a direct result of the work of the center. This phase of the project has proved to be very successful. It has been the experience of the center, however, that while agencies are willing to accept addicts, usually patients discharged from Lexington are unable to make appropriate use of the various existing agency resources when referrals are made on a voluntary basis. It would appear that some other approaches should be tried in the future, such as introducing some form of compulsion to follow through on appropriate referrals.

In the past year the demonstration center has been used increasingly as an informational and consultative resource, answering inquires by interested lay and professional persons and serving a catalytic function in bringing together the leaders of community agencies concerned with drug addiction. It has provided consultation to community agencies and participated in public conferences, seminars, and municipal and voluntary committees interested in formulating programs for the management of addiction.

A second objective of the demonstration center is the followup study of former Lexington patients. An earlier followup study was made by the Bureau of Medical Services during the period of October 1951 to January 1957. The earlier study showed high overall rates of readdiction after discharge. These rates differ, however, with age, sex, ethnic background, length of hospital stay, and possibly other factors. The center is attempting to locate and continue following, for an extended period of time, a sample of 750 from the original group. It is hoped that the continuation of this study over an extended period of time will begin to shed light on when and how and why some of these differences occur.

New York took major steps in 1959 to strengthen its program for drug addicts. A State appropriation of $300,000 was made to open a research facility on drug addiction at the Manhattan State Hospital. This research unit will combine laboratory, inpatient, and outpatient operations. Also, as of January 1959, New York City's Department of Hospitals accepted responsibility for drug addicts who commit themselves voluntarily. The department of hospitals may refer the patient to a mental health clinic in a city hospital or may provide inpatient care. Riverside Hospital, which is also part of New York City's Department of Hospitals, continues to provide inpatient and outpatient care for drug addicts under 21 years of age. The New York State Health Department, State mental hygiene department, and the New York City Community Mental Health Board contribute to the support of the program at Riverside Hospital.

Presently the New York State Department of Mental Hygiene is planning the establishment of two new units for the care, treatment, cure, and rehabilitation of narcotic addicts. An 80-bed inpatient unit to serve the downstate area will be set up at Central Islip State Hospital, Long Island, while the other, a 20-bed inpatient unit will be located at Utica State Hospital, and serve patients in the upstate area.

In Michigan the narcotics clinic of the Detroit City Department of Health was established in 1952 and continued as such until July 1958. Since then the clinic has been integrated into the psychiatric clinic of the outpatient department. Addicts are now admitted to the regular psychiatric clinic. The staff regards narcotic addiction as analogous to tuberculosis, heart disease, and other chronic illnesses in that both adequate treatment and followup are required.

The California Legislature in 1958 appropriated $125,000 for an experimental program for treatment and research relative to convicts who are also addicted to narcotics. A major portion of the treatment takes place at the Chino Minimum Security Prison, which serves also as the admission facility for prisoners from southern California.

As part of the treatment and research program a parole system has been established for the narcotic-addicted prisoner, whereby a condition of parole may become that of participating in the Whittier experimental program. This means that the parolee becomes a member of 1 of 2 groups of approximately 100 each, 1 group receiving either nalline hydrochloride or lorfan tartrate, the other group being the control. Clinics are held each week for each member of both groups, the purpose being to determine the effectiveness of these drugs in the detection, treatment, and control of addiction. If an addict is found to be taking drugs, he may be returned to Chino, not necessarily as a parole violator but as a person in need of treatment.

This year's legislature appropriated an additional $375,000 to the original $125,000 to make possible the opening of similar units in downtown Los Angeles and in San Francisco.

More recently the Governor's special commission on the narcotics problem, after an 8 months' study, called for new State laws permitting virtually unlimited search of the abodes of narcotic suspects—the commission proposing that 1961 be made "Fight Narcotics Year," recommended increased protection for informers, stiffer penalties for narcotics peddlers, and mandatory State hospitalization for addicts.

RESEARCH

Tests of new drugs

Tests of the addiction liability as well as the therapeutic efficacy and toxic effects of new drugs constitute a major part of the continuing research program of the Institute's Addiction Research Center at Lexington, Ky. These studies provide information on the human addiction liabilities of drugs (chiefly potent analgesics with morphinelike properties).

Among others, the Institute tested a new synthetic drug known as I–K–1. This drug is as effective as codeine in relieving pain in humans yet it is less than one-seventh as addictive as is codeine. I–K–1 is, therefore, the closest approach yet made to a nonaddicting analgesic drug. Its addictiveness is so low that it is believed that narcotic law controls will not be necessary. Since codeine accounts for 90 percent of all narcotic usage in the United States, the importance of an essentially nonaddictive substitute for codeine is evident. I–K–1 will probably become available in the American market sometime in calendar year 1961.

Methods for evaluating the addictiveness of new drugs in human subjects were markedly improved during the year. It has been found that the subjective sensations induced by this type of drug in former morphine addicts can be measured quantitatively and the subjective effects induced by new drugs compared with those of morphine or codeine.

Psychological studies

Recent studies have reaffirmed the overwhelming importance of "psychopathic" or "sociopathic" personality traits in addicts. These investigations have further shown that psychopathic traits are found in the same degree in addicts, alcoholics, and in nonaddicted, nonalcoholic criminals.

Neurophysiological studies

Studies at the Addiction Research Center have shown that it is possible to develop tolerance and dependence in dogs and cats in a few hours by continuous intravenous infusions of morphine. This technique may represent a new and simple way of evaluating the addictiveness of new drugs that could readily be used by pharmaceutical companies or universities. Ability to induce addiction in a very short time is also proving to be a powerful tool in neurophysiological studies of addiction.

Psychotomimetic drugs

Since cocaine and marihuana in high dose induce temporary psychoses in some persons, and mescaline, the active constituent of the peyote cactus used by the American Indians, readily does so, studies of such "psychotomimetic" agents are important aspects of research on addiction. Administration of increasing daily doses of LSD–25, psilocybin, and mescaline to human volunteers results in a diminishing psychotomimetic effect (tolerance). Patients who were tolerant to any of these three drugs were also "cross tolerant" to the other two, suggesting that all three drugs induce psychoses by some common mechanism. Studies are being extended to include amphetamines, cholinergic blockers, and synthetic drugs with marihuanalike effect.

Psychopharmacology service center

Research grants awarded through the Research Grants and Fellowships Branch and the Psychopharmacology Service Center include a large number relating to drug addiction.

In the early summer, the Institute was approached by the Illinois Narcotic Control Division as to the possibility of developing a simple, rapid urine test for the presence of opium alkaloids. The division has responsibility for following all identified drug addicts after these individuals have completed prison sentences or periods of hospitalization. At present these postaddicts are being followed by a Nalline test administered at purposefully irregular intervals. If the pupil contracts following administration of 3 milligrams of Nalline, the individual is judged not to be under the influence of heroin or other opium alkaloids. If the pupil remains constant in size or increases in diameter, the individual is suspected of being under the influence of narcotics and chemical tests of the urine are run to determine whether this is in fact the case.

The group from Illinois felt that a simple, rapid urine test for the presence of opium alkaloids would be extremely useful and would be preferable to the present system which depends on the cumbersome and expensive Nalline test and equally cumbersome and expensive urinary determinations. The Institute agreed to hold a meeting of experts in opiate chemistry and opiate metabolism to discuss the feasibility of developing a rapid, simple urine test for opium alkaloids usable by parole officers in the field, and the possibility of improving present methods for the analysis of urines for opiate alkaloids in a central laboratory.

A group of 11 experts in drug addiction and opiate chemistry met at Bethesda on December 16, 1960. The meeting was also attended by scientists connected with narcotic addiction programs in Illinois, California, and New York, the three States with the largest drug addiction problem. The group agreed that gas chromatography was the technique showing the most promise of becoming a rapid and efficient method for the processing of large numbers of urine samples for the presence of opium alkaloids. It was also agreed that the amounts of morphine or heroin, their glucuronides and other metabolites present in the urine of addicts were so small that it was highly unlikely that any simple "clinitest" technique, such as that used to detect sugar in diabetics, could be developed for use in the field.

The group agreed that work on the development of better and more efficient methods for the routine analysis of urines for opiate alkaloids was highly desirable because of the growing volume of work of this sort in States such as

California and Illinois which were closely following identified drug addicts to detect recidivism at an early stage. The further work needed to establish the practicability of utilizing gas chromatography for the routine analysis of urine samples was felt by the group to deserve a high priority.

It was also unanimously recommended that a detailed and systematic study of the comparative sensitivities of the Nalline test, the Mannering method for detection of opiate alkaloids in the urine and the gas chromatographic approach should be carried out, first in a population receiving known amounts of narcotics in a controlled environment, and then on patients receiving known amounts of other drugs likely to produce false positive reactions, and also in subjects known to be receiving no narcotics whatever. Only in this way could the real reliabilities of the various measures be established.

JUVENILE DELINQUENCY

Mr. Fogarty. We gave you a million dollars more that you requested last year to start special research work in the field of juvenile delinquency. How much is budgeted for 1962 along the same line?

Dr. Felix. I don't have the 1962 figures here. The 1961 figure will be a little over $3 million in this area, total expenditures.

I have a report on this which I can supply.

Mr. Fogarty. You may supply that.

(The material requested follows:)

Juvenile Delinquency

EXTENT OF THE PROBLEM

Juvenile delinquency is a problem which merits the serious concern of the people of the United States. The number of delinquency cases disposed of by juvenile courts in the United States has risen for 12 consecutive years. In fact the number of such cases increased by more than three times between 1948 and 1959. And although the child population of delinquency age increased by about a third during this period, the actual delinquency rate per thousand children of delinquency age doubled. It is reliably estimated that one boy in five in this country has a delinquency record by the time he is 18 years old. It can of course, be argued that many of the offenses that are counted in establishing this figure are relatively minor. This is true, but there are other reasons for regarding the official statistics as indicating only the part of the iceberg that shows above the surface. For example, it is reported by the Children's Bureau that for every child who becomes a juvenile court statistic there are two or three who are dealt with informally by the police even though they may have committed similar offenses. In addition, the Federal Bureau of Investigation indicates that for all reported major crimes in the United States only about one in four results in an arrest.

Looking in particular at offenses reported by the FBI in which youth figure prominently, it is observed that about half of all arrests for burglary and larceny involve persons under 18 years of age. Almost two-thirds of the arrests for auto theft involve such persons. Yet in these three categories of offense slightly less than one in four result in an arrest. If juveniles commit a similar proportion of the offenses for which no arrest is made this would mean that the juvenile crime problem in these serious categories is more than double the size indicated by the official statistics. This fact cannot be minimized, since approximately half of all juvenile court offenses by boys are in the theft category. Boys constitute our major juvenile delinquency problem since they outnumber girls by about five to one in this regard.

But there are even more threatening considerations. Even if the delinquency rate levels off, the problem will increase by about 50 percent by 1980 since the child population of delinquency age will increase by about 50 percent in the next two decades. In addition, in the next decades many more of the people of the United States will be living in or near big cities. At present the big city delinquency and adult crime rates are at least three to four times the rural and small town rates. It seems likely, therefore, that as the Nation becomes more urban the delinquency and adult crime rates will continue to rise.

It is true that when traffic offenses are excluded, the national delinquency rate has appeared to be leveling off in the last 3 years. But one cannot tell whether this datum is encouraging until it is determined whether the proportion of recidivists and serious chronic offenders is continuing to increase despite the leveling-off rate. Also, the rate of traffic offenses is continuing to rise, and certainly many traffic offenses constitute serious offenses against public safety.

THE REPORT TO CONGRESS

In view of this situation, in the spring of 1959, the House Appropriations Committee requested the National Institute of Mental Health to collaborate with the Children's Bureau in preparing a comprehensive report for the Congress on juvenile delinquency. The report was submitted in February 1960, and with its appendices constitutes a new source of documentation concerning delinquency. As a result of interest evidenced by both individuals and organizations, one of the appendices is currently being prepared for publication.

NEEDED TASKS

When the report was completed it was apparent that a number of needed tasks must be accomplished if adequate control of the problem is to be achieved.

(1) As indicated in the introduction, national data regarding the extent and nature of the problem is very inadequate at present. When a national rate increase is reported by the Children's Bureau this increase cannot be evaluated in terms of type of offense, proportion of chronic or recidivated delinquency involved, or segments of the juvenile population involved by socioeconomic status, ethnic group, age, family composition, etc. Given the present state of our knowledge, it is difficult to determine how seriously or in what ways such rate increases should be dealt with. If the increase is mainly in the area of minor traffic offenses and the mischievous behavior that is characteristic of adolescents the problem may not be one of national concern. If, on the other hand, the rate increase consists primarily of the more serious offenses as it is believed, and represents an increase in the chronic antisocial type of delinquent, the problem becomes very serious indeed, and requires much different control measures.

(2) It is important that demontration projects be in operation to attack the problem at various stages of its development. Attention needs to be given to early prevention, to early identification of predelinquents, to effective treatment of the first more serious offense, and finally, to the rehabilitation of the chronic offender.

(3) Because of the great shortage of trained personnel in the delinquency field it is important that training projects be inaugurated which develop and test training methods for all types of both professionals and nonprofessionals.

(4) Since there are no widely accepted techniques and instruments for evaluation of the effectiveness of delinquency programs there is need for the development of such instruments both for evaluating small programs aimed at a few individuals and for mass programs which attempt to deal with the problem on a citywide basis.

(5) Another high priority need is for a center in which research and service projects in the field can be described, cataloged, and made available to professionals and nonprofessionals in the field through journals, digests, collections of abstracts, series of monographs, films, etc.

(6) The foregoing needs must be met if the meaning of the problem of the United States is to be evaluated and so that immediate measures for attacking the problem can be undertaken. There is, however, a more systematic long-range approach which requires early inception. This is required because no experienced person in the delinquency field feels that adequate understanding exists at present regarding the processes which are involved in the development of the many different types of delinquents existing in our society. It is important, therefore, that mental health and social science theory relating to juvenile delinquency be structured into as coherent a whole as possible and then divided into areas or subunits which are amenable to scientific attack. Once such areas are identified they can be carefully analyzed by groups of experienced professionals in the field so that appropriate research and demonstration projects can be applied to them.

(7) It is also important that collaboration with private effort in the field be sought, since such agencies as the Ford Foundation, the National Council on Crime and Delinquency, the National Council of Juvenile Court Judges, the American Public Welfare Association, the national police and juvenile police organizations, and others are actively concerned with the problem.

THE CURRENT INSTITUTE DELINQUENCY PROGRAM

Following the submission of the report to Congress, $1 million was earmarked in the 1961 Institute budget for new delinquency projects. This amount was allocated by the Institute as follows: $700,000 for demonstration projects, $200,000 for regular research grant projects, and $100,000 for training projects. In addition, an effort was made to see to it that the activities listed above which are deemed necessary for an effective attack on the problem be inaugurated as soon as possible. Much progress has already been made toward these objectives and it is anticipated that much more will be accomplished by the end of the year. The following accomplishments can be reported at this time:

(1) Pilot investigations are underway in three cities preparatory to undertaking a nationwide study of the extent, trends, and nature of the problem. In addition, negotiations are in process with a national survey organization regarding the conducting of a nationwide study.

(2) A number of demonstration projects are in operation involving approximately $570,000 in 1961 funds. In addition, it is estimated that as much as $600,000 in new grants may be approved for payment from 1961 funds before the end of the year.

(3) More than $100,000 has been allocated for training projects from 1961 funds and approximately $500,000 in applications are being reviewed.

Thus, it is anticipated that during 1961, funds in excess of $1 million will be utilized for new programs in juvenile delinquency.

(4) One large-scale evaluative instrument is being tested in New York City. In this project, valuable information regarding the extent and nature of the problem will be attained as well.

(5) An application for Institute support of a research and information center in the delinquency field has been approved this year.

(6) Theoretical conceptualization of the delinquency problem is being undertaken by Institute staff members, and groups of scientists and clinicians are being organized to consider various research areas in the field.

(7) Active liaison is being maintained with the Ford Foundation, the National Council on Crime and Delinquency, the National Council of Juvenile Court Judges, the American Public Welfare Association, the Council on Social Work Education, and other private agencies concerned with the problem.

Thus far the Institute has allocated over $3 million from 1961 funds for delinquency projects. Approximately $550,000 has gone to completely new projects, and it is estimated that another $700,000 in new projects will be approved for payment from 1961 funds.

In addition to projects centrally concerned with delinquency, there is a large number of others concerned either partially with delinquency or with problems which are highly relevant to our understanding of the problem. Institute staff members have analyzed and classified 108 projects into 11 categories which are either centrally concerned with or highly relevant to the delinquency problem. These categories include normal personality studies, studies of personality pathology, studies of family structure and processes, studies of peer groups, studies of the school and delinquency, studies of various preventive and treatment methods, studies of institutions for the treatment and rehabilitation of delinquents, studies of drug addiction and delinquency, long-term followup studies of delinquents, studies of special types of offenders such as sex offenders and runaways, and studies of multiple service communitywide attacks on delinquency.

Table of obligations

Actual, 1960	$1,927,000
Estimate, 1961	3,074,000
Estimate, 1962	4,343,000

HIGHLIGHTS OF CURRENT PROGRAM

Mr. Fogarty. Give us some of the highlights on what you have been doing this past year.

Dr. Felix. We have at the present time three pilot investigations preparatory to a national survey going on in the United States developing a number of the factors involved in delinquency. One is in Flint, Mich.; one at Quincy, Mass.; and one in New York City.

We also have a number of demonstration projects. One of these which we have discussed before this committee in the past, and at the special hearings you held last year was a project under the name of "Mobilization for Youth in New York City." This group has been given a preliminary grant to get going.

I understand informally that they are moving very well and will probably come in for increased funds.

We are trying to attack this at several levels at once. It has been claimed, as you remember, that many delinquents are psychologically disordered youngsters and that the most effective way to treat them is to treat them psychiatrically. This is certainly true in some cases. As to how many, this is another problem.

The South Shore Guidance Center in Quincy, Mass., is doing a screening study to see how many of the cases are in this category. At the Judge Baker Guidance Center in Boston, they are trying to identify youngsters before they become delinquent. and are trying to deal with them on a treatment basis ahead of time to see if they can prevent delinquency.

At the Quincy, Mass., South Shore Guidance Center they are attacking this in a little different way. They are working with the courts there so that youngsters who are in conflict with the law, who come before the courts—will be referred to the guidance center by the juvenile court judge. They tailor a program for his further care and treatment, which is in conformity with his psychological makeup and with his social characteristics.

In cooperation with the court, they are working in this fashion to see whether a highly individualized type of treatment of the delinquent will prevent further delinquency.

There is a program going on in the predelinquent, chronically disturbed youngsters, inpatient and outpatient, at the Bradley Home in Riverside, R.I., which is developing very nicely.

Mr. Fogarty. Is there anything new that you think we ought to be doing in 1962 in this field?

Dr. Felix. I think if we push present studies—and I have only given you a few of them, if we push these forward another year or so and see what pans out and what doesn't, I will be able to make more definitive recommendations.

My worry is, if we go all out on some projects which have been claimed will do good, before we have fully tested them out, we would waste both money and effort. This is important enough, but this is not really as important as the probability that there would be in the minds of many people that a procedure is good because the Federal Government is supporting it for wide application. This leads to the idea being adopted in more places. If the procedure has not been critically evaluated and is in fact not effective, it is a waste of time and effort and doesn't do the children any good.

So we want to be sure, and I would prefer to move conservatively in this area, because I have heard it over and over again: "Well, the Federal Government must think this is good because it is supporting it." We may think it is promising, but that doesn't mean we think it is good until it proves itself out.

Mr. FOGARTY. I was going to ask some more questions, but I want to give the other members of the committee an opportunity to ask some questions. So will you give us a statement for the record on the following: psychopharmacology, schizophrenia, the population factors associated with mental illness, diagnostic methods, project grants, your work with St. Elizabeths Hospital, and the State control program which is budgeted for $6 million for both 1961 and 1962.

Dr. FELIX. I will be happy to supply that.

(The information requested follows:)

BIOMETRICS

THE PROGRAM OF THE BIOMETRICS BRANCH OF NATIONAL INSTITUTE OF MENTAL HEALTH

The program of the Biometrics Branch is dedicated to the achievement of 3 major goals: (1) improving the adequacy and reliability of statistical data pertinent to the planning and evaluation of national, State, and local programs established to prevent and control mental disorders and to promote mental health; (2) assuring the utilization of appropriate biostatistical methods in laboratory, clinical, epidemiological, and other field research designed to increase our knowledge concerning the many factors related to the attainment of various levels of mental health, the etiology of mental disorders, their incidence and prevalence in various population groups and the effectiveness of therapeutic procedures, prevention and control programs, and (3) developing new and modifying existing biometric, statistical, and mathematical theory and methods to meet special problems encountered in the various research and operational activities represented in the intramural and extramural programs of the Institute and of the various States.

The rapid growth of National, State, and local mental health programs, the increased financial support being given to these activities and the emphasis on clinical, laboratory, and epidemiologic research has resulted in an increased demand for facts and figures relating to these programs and to the distribution of mental disorders in the various segments of the population of the Nation. Collection of the necessary data for program planning and evaluation and for estimating future needs for manpower, clinical services and facilities requires population and epidemiological research in a difficult subject matter field. Because of the broad scope of the mental health problem and its complex nature, the Biometrics Branch has concentrated its efforts, for the time being, on developing for each State a systematic body of uniform statistical data concerning the characteristics and the fate of persons under treatment in mental hospitals and outpatient clinics. This course of action was decided upon for several reasons—first, in our current state of knowledge, it is difficult to obtain data on the incidence and prevalence of mental disorders in the general population of the various States; second, since many State departments of mental hygiene have already developed statistical reporting systems for gathering data on the characteristics of the large number of patients for whom they provide care, it seemed reasonable to make use of these organized data collection activities as a wedge for developing a systematic body of statistical and epidemiologic data concerning the mental disorders in each State.

Considerable progress has been made in the collection of data on patients under treatment in mental hospitals and outpatient psychiatric clinics. The Branch works with the States to improve reporting within public mental hospitals and outpatient psychiatric clinics and to develop special studies around these basic data. The model reporting area for mental hospital statistics now includes 26 member States. The hospitals in these States account for 226 of the 280 State and county mental hospitals of the Nation and provide care for approximately 80 percent of the patients in all State and county mental hospitals on any one day. The goal of the model reporting area is to develop, through cooperative activities of the Federal and State Governments, standards for the collection and analysis of data, basic tabulations and facts that every mental hospital system should have. In addition, various collaborative research projects are developed to clarify the role played by the mental hospitals in the various communities whose populations they serve, to evaluate the impact hospital programs are having on the reduction of disability from mental disorders and to determine the effect new community facilities will have on the characteristics of the patient populations under treatment in mental hospitals. The Branch has developed statistical models which specify types of data needed to quantify more precisely the flow of patients through mental hospitals and to measure annual changes in the patient composition of these hospitals. Data are now being collected which will clarify considerably the impact of the new approaches to the care, treatment, and rehabilitation of the mentally ill. The activities of the model reporting area have stimulated the development of regional groups of mental health statisticians, in the Midwestern and Southern States, who meet to discuss problems of a regional nature and develop plans to solve them. Of particular interest is the emphasis the Southern Regional Educational Board is placing in the training of biostatistical personnel to meet the needs of the State agencies for this type of personnel

Psychiatric clinics have also been assisted in developing methods for reporting data concerning their clinical and community activities. At the start of this program in 1955, 383 of the 1,260 clinics were in a position to report data on such activities. As of 1959, 1,094 of the 1,429 clinics report such information. Regional meetings are held periodically with representatives of all of the State mental health authorities and personnel from individual clinics to review the national reporting program and to consider the modifications in definitions and items of information collected. As a result of these meetings revisions are made as necessary in the format in which data are being reported annually by the States so as to provide greater flexibility and variety in the resulting tabulations and to provide data to meet the changing needs and emphasis of various programs.

The task of collecting data on the fate of patients who receive services in clinical facilities remains an extremely difficult one because of the lack of certain essential knowledge on the etiology and epidemiology of the mental disorders and the absence of instruments that can be used in comparable fashion from institution to institution and from clinic to clinic to determine severity of illness and to characterize the psychologic status, the degree of psychiatric disability, social and familial adjustment, and physical condition of patients at various intervals following onset of disease. As more new therapeutic programs and types of treatment facilities are introduced the task of obtaining pertinent data on people under treatment becomes increasingly difficult and complex, and data derived from separate treatment facilities such as the Veterans' Administration, State and private mental hospitals, outpatient clinics, and psychiatric facilities of general hospitals become increasingly difficult to interpret. It has become quite apparent that State mental health and State mental hospital authorities must develop statistical reporting programs that will coordinate basic data on patients under treatment in all known psychiatric treatment facilities in their jurisdictions which will include appropriate follow-up data on the various classes of patients. The Branch is undertaking pilot studies to determine how best to develop such centralized data-collecting activities for State and local programs.

The professional members of the Branch have also carried out studies of first admission, retention, release, and death rates of patients admitted to the hospital systems of several States and of patterns of clinic utilization specific for such factors as age, sex, diagnosis, marital status, occupation, urban or rural residence, and distance from the clinical facility. Such operational data can provide a firm starting point for planning and evaluating programs related to the control of and reduction of disability from mental disorders. The facts so collected are of value in that they indicate the volume of treatment and rehabilitation facilities available to a community through these resources, the characteristics of persons utilizing them, provide some indication of the success or failure of the programs of such facilities in coping with the problems they handle and point to unmet needs. These data also underscore the knowledge that must be gained to make possible the assessment of the effect of programs of care, treatment, and rehabilitation on the control of mental disorders.

Another facet of the Branch program is the provision of advice and assistance to State and local mental health agencies in research design, data collection and analysis in order to procure much-needed administrative, clinical, and epidemiological information. Well-trained statistical personnel are quite scarce and through this mechanism the Institute makes available to the States the skills of its experts in this area. Because of the basic importance of good records for clinical management of patients, clinical research and administration, continuing efforts are made to assist States in establishing efficient record systems using comparable terminology and definitions.

The Branch plays an important role in clinical and basic research. To accomplish this it employs a staff of well-trained mathematical statisticians and a mathematician to assist and consult with investigators on statistical, mathematical, and biometrical problems arising in various investigations carried out in the laboratory and clinical sciences at the National Institute of Mental Health as well as by scientists who are working in mental health problems outside the Institute. These services provide the scientists engaged in research in such disciplines as physical chemistry, physiology, psychology, sociology, psychiatry, and social anthropology with the most efficient and valid statistical techniques available in the design and analysis of data, planning of sample surveys, and development of mathematical models. This staff provides liaison services between investigators in the laboratories and branches of the Institute, who collect large bodies of data, and the machine programers of the electronic computer. In addition, research in mathematical statistics in several different areas is being vigorously pursued to develop methods to increase the efficiency and logic of design of experiments in the mental health field.

The work of the Branch has gained attention both nationally and internationally. The Chief of the Branch serves on several national committees concerned with epidemiologic and operational research on the mental disorders, nomenclature, and classifiaction of mental disorders. He has also served on several study groups of the World Health Organization as well as acting as a consultant for the World Health Organization to the Governments of Australia, Philippines, Taiwan, and Japan on the organization of programs of statistical and epidemiologic services for their programs of the control of mental disorders. Several of the staff have also been invited to serve as visiting professors in the departments of statistics of several of our leading universities and serve on various research grant committees.

The increasing emphasis being placed by Federal, State, and local governmental officials on expanded programs and new approaches to prevent and control disabilities resulting from mental disorders and on the need for basic and applied research in the many sciences related to the mental health field will create additional demand for the services of skilled biometricians. They will be needed to produce data for guiding program planning and evaluation, for designing experiments and formulating mathematical models which can elucidate the underlying phenomena being studied. It is anticipated that the Biometrics Branch will be called on to play an increasingly important role in this endeavor.

PSYCHOPHARMACOLOGY SERVICE CENTER PROGRAM

INTRODUCTION

During the past year several special programs have been developed which will markedly improve the clinical drug evaluation aspects of the psychopharmacology program of the National Institute of Mental Health. Interesting new research findings have continued to evolve from both the basic and clinical research projects already underway under grant support. In addition, expanded services in the areas of data analysis and scientific information are being made available to investigators in psychopharmacology.

In order to provide a better overview of the place of these developments within the broader field of psychopharmacology, they will be discussed within the context of such subareas as clinical drug evaluation, basic psychopharmacological research, and Psychopharmacology Service Center staff activities.

CURRENT CLINICAL RESEARCH

Phenothiazines and other tranquilizing drugs

There are now 10 phenothiazine derivatives available for prescription use in the treatment of psychiatric conditions. All these drugs are recommended by the manufacturers for use in the treatment of schizophrenic symptomatology. Are these drugs different from one another in effectiveness? Do they differ from one another in the specific types of symptoms affected? Are any of them superior to the original drug in this group—chlorpromazine—in general efficacy or in specific effectiveness in the treatment of individual symptoms? The answers to these questions have been slow in coming and definitive answers are still not available although recent findings show interesting trends.

First, it is clear from grant-supported studies at Spring Grove State Hospital and at the Downstate Medical Center in Brooklyn, N.Y., as well as from the Veterans' Administration's multihospital studies of psychoactive drugs, that chlorpromazine is substantially more effective than promazine in the treatment of schizophrenic states. Work at Spring Grove State Hospital and work carried out by the Veterans' Administration has also indicated that chlorpromazine is more effective than mepazine in the treatment of schizophrenic symptoms. The investigators at Spring Grove State Hospital report that their study fails to show mepazine to be different from inert placebo in its ability to alter psychotic symptoms. A number of investigators report that several of the other newer phenothiazines—perphenazine, prochlorperazine, thiopropazate triflupromazine, and trifluoperazine—have appeared on the basis of uncontrolled early clinical trials to be effective in the treatment of schizophrenic symptoms at lower doses than chlorpromazine. It has yet to be shown, however, that any of these drugs possess specific advantages over chlorpromazine in their ability to reduce psychotic symptoms when used at appropriate dosages. Results from a multidrug controlled comparative study carried out at Spring Grove State Hospital and from the Veterans' Administration's most recently completed controlled cooperative drug study show a tendency for triflupromazine to be somewhat superior to chlorpromazine in overall clinical efficacy. A study recently completed at Spring Grove State Hospital has shown a tendency for prochlorperazine and perphenazine to be a little less effective than chlorpromazine. Perphenazine was found likely to produce undesirable neurological side effects. The group at Spring Grove State Hospital is now proceeding to compare chlorpromazine and triflupromazine with the other newer phenothiazines: thiopropazate, trifluoperazine, thioridazine, and fluphenazine.

A large-scale comparative study of the effectiveness of chlorpromazine, prochlorperazine, perphenazine, and triflupromazine and placebo in chronic schizophrenic patients has just been completed at Napa State Hospital and the data are being analyzed. Preliminary results as reported by the investigators indicate that these drugs, as a group, are very much more effective than placebo in producing symptomatic improvement and in enabling patients to be returned to the community. More refined analyses now underway will provide evidence concerning qualitative differences between these drugs.

One of the most interesting new phenothiazines is thioridazine. This drug produces substantially no neurological side effects common to other clinically potent phenothiazines. Preliminary studies carried out by grantees working at the Palo Alto Veterans' Administration Hospital and the Nebraska Neuropsychiatric Institute support the thesis that this drug is at least as potent as chlorpromazine in he treatment of chronic schizophrenic patients and is less likely than chlorpromazine to produce neurological side effects.

Many investigators have suggested that to be effective in the treatment of psychotic symptoms, a phenothiazine must produce unpleasant neurological side effects. The systematic study of the relationship between the production of neurological side effects and clinical potency will have both specific practical implications for the use of existing drugs and for the development of newer and more effective phenothiazines. For this reason, the Psychopharmacology Service Center, on the recommendation of the Advisory Committee on Psychopharmacology and the National Advisory Mental Health Council, has developed a nine-hospital cooperative study of the effectiveness of three phenothiaine derivatives—thioridazine, chlorpromazine, and fluphenazine—in the treatment of acute schizophrenic patients. Of all the phenothiazines now in general clinical use, thioridazine is the least likely to produce neurological side effects and fluphenazine is probably the most likely to do so. It is important to determine whether either drug possesses clinical superiority over, or qualitative differences from, chlorpromazine. The study now underway will, in addition, provide valuable information concerning the differential responsiveness of male and female patients to the three drugs. Since the nine hospitals have been selected to represent a broad spectrum of clinical treatment milieu, ranging from private hospitals and university psychiatric pavilions to psychiatric wards in city hospitals and the admission services in State hospitals, the study will cast some light on the relative effectiveness of drug treatments in different hospital environments and will provide the first systematic data relevant to the long-standing question, "Are drugs more effective in public mental hospitals than they are in university psychiatric pavilions?" The broad range of psychiatric hospitals involved will also insure that the final results will be more representative of the true effectiveness of these drugs than would results obtained from studies in a single hospital or in a more homogeneous group of hospitals.

The need for this multihospital study involving a variety of hospital milieu has recently been underlined by a report from a grant-supported study carried out at a very well staffed and equipped psychiatric facility which failed to show either chlorpromazine or reserpine to be superior to an inert placebo in the treatment of recently hospitalized psychiatric patients for whom tranquilizing medication appeared indicated.

The results of the multihospital study will complement the results obtained from a concurrent cooperative study being carried out by the Veterans' Administration, studying newer phenothiazine derivatives in male schizophrenic patients newly admitted to Veterans' Administration hospitals. Since the population studied by the Veterans' Administration is likely to be somewhat more chronically ill than the population in the nine-hospital study described above, it will be important to see whether the results obtained in the two studies are or are not the same. Since both cooperative studies will utilize a common clinical rating instrument, the Lorr scale, it will be possible to determine whether Veterans' Administration patients differ significantly in type or severity of psychiatric symptoms from patients newly admitted to State or private mental hospitals.

Well-designed controlled studies of the effectiveness of meprobamate and other drugs used in the treatment of neurotic outpatients have to date produced conflicting results. Some studies show meprobamate to be superior to an inert placebo while others fail to show any difference between the two treatments. On the basis of some data from a study carried out at Johns Hopkins it would appear that significant differences may exist among therapists in the response of their patients to meprobamate and to placebo. To examine this problem more directly, a special study of the effects of the therapist's behavior on the response of neurotic outpatients to meprobamate and placebo is now underway. The study was planned by the Psychopharmacology Service Center in cooperation with investigators at the University of Pennsylvania and Johns Hopkins University. The psychiatric outpatient units of both institutions are participating in this study. This study will be the first to formally test the hypothesis that physicians with a high level of therapeutic ardor induce greater improvement in drug-treated patients than do physicians whose attitude is more reserved and experimental. Further, it is hypothesized that the difference between drug- and placebo-treated patients will be greater in the patient groups treated by the therapeutically positice physicians. This special study is a portion of a larger special program which is concerned with the efforts of psychological set and social interaction upon drug response in both patients and normal subjects.

A group of grant-supported investigators at the University of Michigan have studied the effects of three substances: (1) Meprobamate, the most widely prescribed mild tranquilizer; (2) a combination tablet advertised as a tranquilizer and sold without prescription; and (3) placebo, in a group of anxious neurotic subjects and a group of normal college students. Although the combination tablet contains many substances in small amounts, its alleged "tranquilizing" properties are probably attributable to its bromide content. The study showed that five tablets a day produced a significant rise in blood bromide level and occassional skin reactions of the type usually associated with bromide ingestion. Both the combination tablet and meprobamate produced greater sleepiness than did placebo, and with both drugs patients felt that more physical effort was required to carry out daily activities. Under meprobamate, patients appeared to the observing psychiatrists more rested, less tense, and to have improved psychological functioning. The combination tablet, on the other hand, appeared to produce impairment in such psychological functions as concentration and retention. Observations by the subjects' friends also suggest that meprobamate produced an observable decrease in anxiety level, while the combination ablet principally reduced activity level. In summary, meprobamate was shown in this study to be superior to the combination tablet, a bromide-containing patent medicine, and to an inert placebo, in decreasing anxiety level in anxious patients and in improving psyschological functioning, whereas the combination tablet tended to slightly impair psychological functioning without providing comparable decreases in observed anxiety. Both drugs produced some sedative effect.

A study of the effects of perphenazine, a phenothiazine, on the verbal productions of psychosomatic patients at the University of Cincinnati has shown that the drug causes a significant decrease in both overt and covert manifestations of hostility in the total patient group. Patients with substantial amounts of anxiety also showed a decrease in this symptom, and the patient group as a whole showed a significant increase in feelings of general well-being resulting from treatment with the drug.

A series of studies of drugs used in the treatment of neurotic, hyperkinetic and sociopathic children in the outpatient clinic at Johns Hopkins University has shown that neurotic children show such a high rate of improvement on placebo that no significant drug effect can even be expected. Sociopathic children have shown little or no improvement on any of the drugs (meprobamate, prochlorperazine or perphenazine) studied to date. The first two drugs showed little effect on hyperkinetic children. The effects of perphenazine were equivocal. The rate of improvement was not significantly greater than that obtained under placebo, but those hyperkinetic children who improved under perphenazine became worse when the drug was discontinued. The investigator who has carried out this research believes that further research may well identify drugs which will be effective in the treatment of hyperkinetic disorders of childhood. This research underlines, however, the present general ineffectiveness of drugs in psychiatric disorders of childhood with generally proven efficacy in adult psychiatric patients.

Antidepressive drugs

A research project utilizing depressed patients from four New Jersey State hospitals is now comparing electroconvulsive therapy, iproniazid and an inert placebo in a detailed controlled study. Preliminary results on the first half of the total patient sample to be studied reveal two important findings. First, most of the depressed patients in this study which is, to date, restricted to women between ages 20 and 40, tend to show significant improvement even on placebo medication. Second, both electroconvulsive therapy (ECT) and iproniazid show some qualitative differences from placebo. ECT has shown overall superiority in total symptom reduction while iproniazid produces a significant speeding of psychological functioning. A similar study comparing imipramine, phenelzine, isocarboxazid and ECT is underway in three Massachusetts State hospitals. A preliminary analysis of the data from this study is now being carried out. Several other smaller clinical studies of antidepressant drugs are also in progress.

Early clinical drug evaluation

Five grant-supported units are now actively engaged in the systematic early clinical evaluation of new drugs. Although these units have provided some useful preliminary information on such important newer drugs as thiroidazine, imipramine, fluphenazine, and the monoamine oxidase inhibitors, the work now in progress falls far short of meeting the needs of the field of psychopharmacology for the expansion of research effort in this special area. Animal drug-screening techniques can still provide only very tentative information about a drug's therapeutic possibilities. All recent discoveries of new types of psychiatric drugs have been made by clinicians on the basis of studies carried out in patients.

Although the safety of new drugs and their ability to affect behavior or central nervous system activity may have been established in experimental animals, their special therapeutic properties have been first suggested by their effects in patients. An expansion of support for early clinical drug evaluation should, therefore, facilitate the discovery of other new and important drugs. In addition, the expanded support of such units should help meet the present urgent need that promising new drugs receive a more thorough clinical evaluation as an earlier stage of their development than has generally been possible heretofore.

For these reasons a special program of grant support for early clinical drug evaluation units has been developed and formally announced. More than 20 grant proposals requesting support under this program had been received as of January 1, 1961, reflecting a high level of interest in work of this sort on the part of clinical investigators.

PRECLINICAL RESEARCH

An interesting comparison of four psychotomimetic agents lysergic acid diethylmide (LSD), sernyl L-(phenylcyclohexyl) piperidine HCl), mescaline and ditran (a mixture of N-ethyl piperidine and N-ethylmethyl-pyrollidine), has been carried out in schizophrenic and sociopathic psychiatric patients at Ypsilanti State Hospital. Only one of these, ditran, produced a clear reactivation of previously experienced acute psychotic symptoms in chronic schizophrenic patients and a delirium-tremen-like syndrome in alcoholics with a past history of delirium tremens. Sernyl produced either confused excitement or sedation, without hallucinations or other psychotic symptoms. LSD produced visual illusions and hallucinations, but these were milder than those elicited by ditran and were recognized as drug effects by the patients. Symptoms produced by ditran were not so recognized. Mescaline, in the dosage used, was almost entirely lacking in psychotomimetic properties. The investigators also observed that the effects of sernyl could be effectively suppressed by intravenous succinate. Ditran is presumed to produce psychotomimetic effects because of its potent anticholinergic properties. This theoretical mechanism of action was strongly supported by the finding that tetrahydroammacrin (THA), an Australian drug with marked anticholinesterase activity, effectively blocked the severe psychotomimetic effects of ditran. This research group is now examining THA to see if it has any clinical utility in the treatment of psychiatric patients.

Deanol, a drug being marketed for use in the treatment of mild depressive reactions, has been hypothesized to exert its effect by increasing the amount of acetylcholine in the brain. Doubt has been cast on this theory by a study of the drug by investigators at Yale. They have been unable to produce a significant increase in acetylcholine levels in the brains of experimental animals with this drug.

A study of the effects of dextroamphetamine, meprobamate, and placebo carried out on psychiatrically normal aged male veterans at the Veterans' Administration Center in Martinsburg, W. Va., has shown that both drugs cause significant decreases in the clear-thinking factor of the Clyde mood scale. It is interesting that these aged subjects reported both drugs as producing undesirable effects while studies of younger subjects using the Clyde mood scale have reported generally pleasurable effects from both drugs.

A group at the Massachusetts General Hospital has studied the effects of amphetamine and secobarbital on the athletic performance, judgment, and mood of athletes. The most important findings was that athletes under secobarbital showed poorer performance while judging themselves to be performing better than usual. This disparity between the subjectivity perceived and the real effects of the drug could produce dangerous consequences in individuals who drive under the influence of this and related drugs. Amphetamine, on the other hand, significantly improved athletic performance; the athletes showed a slight tendency to believe they had done less well than had actually been the case.

Grantees at the State University of Iowa have been studying central nervous system activity as influenced both by lesions and by drugs and have been interested in drugs which produce predictable changes in both central nervous system activity and behavior. One compound, tremorine, elicits a continuing rest-type tremor in the cat. They have identified the site of action of this compound and are using this well-understood drug effect as a method for gaining further information about the sites of action of other psychopharmacological agents which influence the drug-induced tremor produced by tremorine. Another compound, imino-beta, beta^1-diproprio-nitrile, has been found to produce a peculair circling and waltzing behavioral effect in mice which can be reversed by certain psychopharmacological agents. Both compounds produce abnormalities of braining function and behavior against which other psychopharmacological agents can be tested. One of the basic problems facing psychopharmacology has been the necessity of using the effects of drugs on the behavior of normal animals as the major approach to the identification of drugs which may be effective in treating abnormal states in man. Drugs like tremorine and imino-beta^1-diproprio-nitrile, by creating specific abnormal behavioral states in animals, may form the basis of promising new approaches to the screening of psychiatric drugs in behaviorally abnormal animals.

Investigators at Yale have prepared an outstanding review article on the effects of drugs on motivation in animals. The article incisively points out the many confounding variables which may complicate animal behavioral studies of drug effects, and underlines the need for using multiple approaches to clearly demonstrate specific drug effects on anxiety, fear, conflict, learning, etc., psychological functions which appear on the surface to be simple and straightforward, but are in reality highly complex. For example, work at Yale has followed up work done earlier at Northwestern which had appeared to show that alcohol prevented an experimentally induced neurotic conflict from interfering with hunger-motivated behavior in cats. The group at Yale has shown that this type of experimental situation must be separated into two components—a hunger-induced drive to approach the food and a fear-induced drive to avoid the food box where, the animal has learned, he will be punished. They have clearly shown that the strength of the hunger drive was unaffected by alcohol, while the fear-motivated avoidance drive was significantly reduced by alcohol. The group at Yale feels that these results obtained in the rat may help to explain some of the paradoxical social effects of alcohol; e.g., a person, whose fear or anxiety has made him repress underlying hostile tendencies, will when drunk, be more inclined to be overtly hostile, while a person with strong underlying amorous drives which are repressed because of anxiety or fear, will, under alcohol, become overtly affectionate.

The studies by the Yale group on tranquilizing and sedative drugs also serve to underline the problems of studying in animals the anxiety- and fear-reducing properties of drugs. For example, chlorpromazine, a potent tranquilizer, appears to have fear-reducing properties when studied in a situation in which the rat must choose between continuing to push a lever for food and retreating to a safe "island" in the cage after being warned by a sound that a painful shock is imminent. It also increases the animal's ability to keep on pressing a bar for a food reward in the presence of a sound which precedes a painful and escapable shock. On the other hand, chlorpromazine does not increase the hungry animal's ability to run down an alley to get a food reward when he knows he will receive a painful shock toward the far end of the alley. Alcohol, on the other hand, markedly alleviates the decrement in alley-running performance produced by fear of a painful shock, but has little or no effect on the animal's ability to keep from retreating to a safe "island" well in advance of an incipient shock and has only a modest ability to maintain food-getting activity during the warning period before an unavoidable shock occurs. Sodium amytal, a barbiturate, is quite effective in maintaining hungar-motivated behavior and in suppressing the effects of "fear" in all three of the experimental situations described above. The relationships between the different effects of these three agents under the three "anxiety" producing procedures described above and their effects on normal, psychoneurotic and psychotic human subjects remain to be determined.

Contracts

A contract for the synthesis of chemical compounds related to serotonin has been awarded and is now in its second year. These compounds are currently being utilized by several grant-supported investigators, as well as by several scientists in the Natioinal Institute of Mental Health and the National Heart Institute. One compound synthesized under this contract, kynuramine, has formed the basis of a new and simplified method for the determination of monoamine oxidase (MAO) inhibition. This method, developed by an investigator in the National Heart Institute, now places such determinations within the scope of the usual clinical laboratory available to clinical investigators in most well-equipped hospitals. Previous methods for measuring MAO activity in man required elaborate and complex instrumentation not generally available. Since several antidepressive drugs appear to act through their MAO-inhibiting properties, this new technique provides a simplified method for determining whether patients treated by these drugs are being given a sufficient dosage to achieve the desired pharmacological effect.

A contract has also been awarded for the synthesis of a number of phenothiazine derivatives which have been tentatively identified as naturally occurring metabolites of chloropromazine and other phenothiazines in general clinical use. The availability of modest amounts of such compounds with proven chemical structure will greatly facilitate research on the metabolism of phenothiazine derivitives, since the small amounts of these metabolites isolatable from the urine of patients or animals make positive identification impossible when standard compounds of known structure are not available.

In the two contracts described above and in the subsequent developments of this program, the aim is to support the initial synthesis of chemical compounds which are needed by grant-supported investigators in psychopharmacology and are not available through the usual commercial channels. Once the syntheses have been completed and small amounts of the substances have been made available to interested grantees and research workers at the National Institutes of Health, it is hoped that additional amounts of these compounds will then become readily available through usual commercial channels.

Informational activities in psychopharmacology

The Scientific Information Unit is continuing its effort to facilitate and improve communication of research findings in the field of psychopharmacology. During the year a large number of bibliographies and reference lists were compiled and distributed. Examples are reference lists on the following drugs: pheniprazine, nialamide, phenelzine, triflupromazine, amphenidone, iproniazid, chlormethazanone, and imipramine. Bibliographies on "research methodology in clinical psychopharmacology," and "placebo problem in psychopharmacology" were compiled as one contribution to the center's mission if improving the quality of clinical investigations of drugs. Information on the pharmacological action of drugs was provided in a detailed and annotated bibliography on the metabolism of, and analytical methods for, phenotheiazine derivatives used in psychopharmacology. In addition, a large number of bibliographic searches were done, and reference lists compiled in answer to specific inquiries.

The collection of documents, including reprints, books manuscripts and monographs has expanded considerably. There are now approximately 12,000 documents on file. Much of the activity of the Unit has been devoted to searching the scientific and medical literature, collecting the documents, cataloging and indexing them, and maintaining the document collection. The collection has been used constantly by members of the center staff and has been of great assistance to them in providing background information necessary to the special projects on which they are working.

With the increasing number of new chemical compounds of importance to psychoptharmacology, it has been imperative to have speedy access to information about them. One major project completed during the year was the establishment of a complete and cross-referenced file of all drugs relevant to psychopharmacology. For each drug, information has been obtained on its chemical formula and structure, chemical name, generic or common name and trade names used in the United States and in other countries. Each drug is also keyed by code number to the document collection, making it possible to retrieve all pertinent reports on it. Maintaining this file will be a continuing activity of the Unit.

Because the document collection and dissemination of information encompasses materials in all languages, it has been necessary to provide extensive translation services, both for indexing purposes and for complete translation of documents. The Slavic languages generally present the greatest problems. An expert in Slavic languages was, therefore, added to the staff, and translations of Russian articles are now available.

The Psychopharmacology Service Center Bulletin is one of the chief means by which information has been disseminated. The bulletin is now sent to approximately 3,500 investigators in the field of psychopharmacology, of whom approximately 1,500 are located outside the United States. Of special interest during the past year were the issues devoted to an annotated listing of all Institute grants in psychopharmacology and a tabular presentation of drugs used in psychiatry. The table listing the drugs was especially well received; over 5,000 copies have been distributed, many of them for teaching purposes in medical schools.

Data analysis

During the past year the Psychopharmacology Service Center has been able to expand its facilities for the statistical analysis of data from psychopharmacological studies. This expansion will make possible the rapid and efficient processing of data coming from the nine-hospital collaborative study of phenothiazines in acute schizophrenic patients. It will also speed the analysis of data from many other studies of special interest to the center and make possible many types of statistical analyses which have not been possible in the past.

Conferences and meetings

A meeting on drugs and community care was organized by the Psychopharmacology Service Center and was attended by some 68 scientists, many of whom were grantees engaged in the study of the effectiveness of drug treatment in the maintenance of psychotic patients in the community. The proceedings included the reports of research results by a number of these investigators and detailed descriptions of a variety of methods utilized by investigators for the assessment of the psychiatric status and the social adjustment in the community of patients released from the hospital. Other aspects of research design in this area of research were also discussed. The research results reported at this meeting provided strong evidence concerning the effectivness of tranquilizing drugs in maintaining schizophrenic patients in the community and in averting their return to the hospital when relapses occurred.

A similar meeting of grantees and other appropriate research workers and consultants interested in the evaluation of drug therapies for depression is planned for the coming year.

SCHIZOPHRENIA

INTRODUCTION

Schizophrenia is a major medical and social problem in the United States. Its incidence is estimated at from 1 to 3 percent of our total population, the majority of the cases occurring during the most productive years of life. More than half of the patients hospitalized for mental disorders are diagnosed as schizophrenic; they occupy one-fourth of all hospital beds in the United States.

In full recognition of the gravity of schizophrenia as a public health problem, the Institute has continued to extend its support for research, training, and service activities which will assist in the prevention and treatment of this disorder.

THE RESEARCH GRANT PROGRAM

During the years in which the Institute has sponsored its research grant program, schizophrenia has consistently called forth a higher investment of grant funds than any other area of special interest to the Institute.

The size and range of the grant program in schizophrenia testify to the continuing obscurity of etiology and limited effectiveness of present treatment methods. The length of hospitalization for schizophrenia in the United States presently averages 13.1 years. Schizophrenia is a group of psychotic reactions which are characterized by fundamental disturbances in reality relationships and concept formations, with emotional, behavioral, and intellectual disturbances in varying degrees. The disorders are marked by a strong tendency for the patients to retreat from reality, by emotional disharmony, unpredictable disturbances in thought, regressive behavior, and, in some, by a tendency to "deterioration."

Many research investigators today feel that it is unlikely any one cause of schizophrenia will be identified. Rather the complexity of this condition has suggested many possible etiological agents, multiple biological, psychological, and social factors, the complex interplay of which may result as schizophrenia. Recent overviews have indicated that the most urgent problem is the development of new and more useful diagnostic categories in schizophrenia, together with a conceptual scheme which will allow investigators to view the multiple factors involved in a single framework to accommodate all the factual findings and permit better understanding of their relationships. Such a framework for current research in the broad area of schizophrenia, including studies in phychophysiology, neuroanatomy, genetics, endocrinology, biochemistry, psychology, and sociology, is emerging slowly and is linked increasingly with understanding from dynamic psychiatry.

The following brief descriptions indicate some of the major areas in which research projects in this field are being supported.

Psychopharmacology

Overwhelming evidence confirming the efficacy of phenothiazine derivatives in the treatment of both chronic and acute schizophrenic reactions continues to accumulate. Results from studies supported by the Institute, as well as from the Veterans' Administration's series of cooperative studies of drug treatment of schizophrenic patients, indicate that although a number of new drugs are being tested, chlorpromazine is still one of the most effective developed to date. The Institute has recently organized a nine-hospital cooperative study of the effectiveness of the phenothiazines in acute schizophrenic reactions, which will provide detailed evidence on differences between two of the most promising newer phenothiazines, thioridazine and fluphenazine, and chlorpromazine. It will also provide evidence concerning the effect of differences in hospital milieu on patient response to these drugs. The hospitals participating in the study include private psychiatric hospitals, the psychiatric services of city hospitals and State mental hospitals.

A special program for the expanded grant support of units engaged in the intensive early clinical evaluation of new psychopharmacologic agents has recently been developed by the Institute. Much of this work will be carried out with schizophrenic patients, and the program is expected to speed the identification and the thorough testing of new drug treatments for schizophrenia.

Research evidence accumulated during the past 2 years has provided positive evidence that maintenance drug therapy is effective in stabilizing chronic schizophrenic patients in the community at a satisfactory level of social adjustment and in preventing relapse and rehospitalization of such patients.

Interesting work on the psychotomimetric agents is also in progress. Recent reports by grantees indicate that a new psychotomimetic agent, produces a severe psychotomimetic state with both auditory and visual hallucinations and with extreme disorganization of thought. In comparison, the psychotomimetic effects of LSD (lysergic acid diethylamide) are much less dramatic. One grantee has described this agent as re-creating in chronic schizophrenic patients the same psychopathology which had been experienced by them in earlier and more fluid stages of their illness.

During 1960, 87 grants, totaling over $2½ million, and which dealt with psychopharmacological aspects of schizophrenia, were supported by the Institute. It is anticipated that this ongoing body of research on the effectiveness of drug treatment of schizophrenia and the nature of drug-induced schizophrenic-like states will be increasingly productive, actively assisted by the research programs described above.

Hospitalization and rehabilitation

While the use of psychopharmacologic agents offers increasing hope that schizophrenic patients may obtain early release from mental hospitals, current research studies continue to seek other improved methods of hospital care.

The sensitivity of schizophrenic patients to their hospital environment and the role of that environment in their recovery or relapse has been recognized by many research investigators. A battery of research studies are presently inquiring into many aspects of the mental hospital milieu and its role in treatment. Among these projects are studies of social structure and adaptation in the mental hospital, studies on the institutional structure of the public mental hospital, of institutional climate and accessibility to treatment, and studies of psychologic change in the hospitalized mentally ill. Increasingly, social scientists are contributing to an understanding of social interaction in the hospital through studies dealing with such subjects as the institutional structure of public mental hospitals as they reciprocally influence and are influenced by treatment programs, studies of patient's social adaptation to mental hospitals, and research analyzing the role of patient-staff relationships.

More and more emphasis is being placed on the use of "open" or "day" hospitals in the treatment of schizophrenic patients as well as on community programs of rehabilitation. The Institute, both in its regular research grant programs as well as through the mental health project grant program, has undertaken support of broad-scale research to evaluate such care. A number of such projects are designed to provide community followup studies of discharged patients, assessment of the community aspects of psychiatric rehabilitation, evaluations or day-hospital care of schizophrenic adults, as well as pilot studies of day nursery school care for schizophrenic children. Other research is examining the rehabilitative potential of special summer camping programs as well as general evaluation of discharge, planning and community followup programs for the mentally ill.

It has been increasingly recognized that aftercare and rehabilitation procedures may play a significant part in the released mental patient's ability to cope more effectively with his environment. The Institute's research program should continue to contribute to pragmatic understandings of the potential of posthospital care for schizophrenic, as well as other, mental patients.

Psychotherapy

Although psychopharmacologic agents and hospital care are important adjuncts in the treatment of schizophrenic patients, research in the use of psychotherapy with both acute and chronic patients has attracted a growing number of investigators. The dynamic psychotherapy of schizophrenic patients has been more widespread in the United States than elsewhere; it is now also increasing in Europe. Recent research continues to indicate that intensive psychotherapy may not only prove very helpful to schizophrenic patients (often in conjunction with or following the use of tranquilizing agents) but may also prove to be an avenue in understanding the schizophrenic process as a whole. During 1960 there was published the proceedings of a substantial symposium, supported by the Institute, which examined at length the outpatient treatment of schizophrenia. Members of this symposium noted particularly the significance of the psychotherapist's empathy with the patient combined with control and competence on the part of the therapist. Still another Institute-supported project resulted during 1960 in a substantial monograph which explored in detail the role of the psychotherapist in the treatment process.

Among the other grant-supported research studies dealing with the psychotherapy of schizophrenic patients are projects examining the long-term effects of psychotherapy and studies comparing, in State hospital settings, the effectiveness of individual psychotherapy alone with drug therapy plus psychotherapy, and of drug therapy alone.

Convulsive and surgical therapies

Recognizably, the variety of methods used in the treatment of schizophrenia reflect the variation in etiological concepts of this disorder. Somatic treatment methods attempt to cure or ameliorate psychiatric conditions by physical approaches to what has been termed the biological substratum of the mind. In addition to pharmacotherapy, discussed earlier, such approaches have included electroshock, insulin shock, and psychosurgery.

The use of psychopharmacologic agents, often combined with psychotherapy, has taken the place of shock treatment in many hospitals throughout the United States. However, Institute-supported research investigators are continuing to explore the effectiveness of the various convulsive therapies.

Many clinicians would like to find a simple method for determining which patients would benefit most from the use of the various therapies. One grantee, conducting a long-range program investigating the relation of personality to type of mental illness and choice of therapy, reported during 1960 on the results of the use of the Rorschach and other psychological tests as predictors for electroconvulsive therapy response. Results of a trial with 87 hospitalized patients indicated that those who subsequently improved after electroconvulsive therapy revealed a basically conventional and unimaginative personality, in general lacked empathy and introspectiveness and had difficulty in communicating verbally. Such findings are yet only suggestive. More information must be gathered on overall personality patterns of psychotic patients before and after various treatments before conclusive evidence for predicting response to treatment can be presented.

The discovery that certain drugs will produce convulsive therapy seizures equivalent to electroconvulsive therapy has also led to comparative testing of the effectiveness of agents like indoklon as opposed to electroconvulsive therapy. At the Spring Grove State Hospital in Maryland, Institute-supported investigators have found indoklon a safe alternate treatment procedure to electroconvulsive therapy.

Other research studies of the convulsive therapies are examining perceptual changes induced by electroconvulsive therapy and the relation of syntactic language changes to postelectroconvulsive therapy conditions.

With the decreasing use of psychosurgery in the United States, fewer investigators are interested in pursuing research on lobotomy. Those projects which the Institute presently supports in this area revolve about followup studies and behavioral and intellectual measures of surgically treated schizophrenics.

The biology and bochemistry of schizophrenia

A large share of the Institute's grant program supports research projects related to the biology and biochemistry of schizophrenia. As many present-day investigators have rejected the belief that schizophrenia is a disease entity of single causation, clues to a multiple etiology of this mental syndrome are currently being sought in gentics, in biochemistry, physiology, endocrinology, and other biological and medical sciences.

Although relatively few Institute-supported research investigators have carried out genetic studies of schizophrenia, evidence for a genetic influence in schizophrenia has accumulated from family and twin studies, suggesting that unevenly distributed individual genetic differences may be of considerable importance in schizophrenic syndromes. This is not to conclude that all such syndromes have a genetic origin. The many methodological obstacles for the genetic study of schizophrenia contribute to the paucity of current research in this area. As one of the country's leading physiologists has observed: "Although the evidence for the great importance of genetic and therefore biological factors in the etiology of many or all of the schizophrenias is quite compelling, the signposts pointing the way to their discovery are at present quite blurred and * * *, illegible." It remains to be established in what forms hereditary factors play a part in schizophrenia and how significant is a factor of hereditary "vulnerability." The Institute has in the past supported twin sudies of schizophrenia and currently underwrites several projects dealing with genetic factors in psychiatric disorders and studies of mating and fertility patterns of schizophrenic families.

Meanwhile a wide range of studies are actively exploring, under Institute grant support, other biological and biochemical aspects of schizophrenia. Among these are included studies of cerebral physiology and functional disorders, study of metabolic patterns and their relation to schizophrenia, immunochemical investigations of schizophrenia, studies of tryptophan in brain function and mental disease, histamine metabolism in schizophrenic patients, cerebral metabolism of neurohormone precursors, pathological chemistry of brain glycolipids and biologically inactive catechols in mental disease.

A variety of biochemical etilogies of schizophrenia have been proposed at one time or another, including autointoxication (particularly through intestinal products), disturbed oxidative metabolism, sensitivity to androgens, faulty detoxification of substances, abnormal betabolisms of amines, diminished adrenal responsiveness and abnormal epinephrine metabolism. As may be observed from the titles of a number of Institute-supported studies cited above, a considerable body of research is underway which is based on the premise that schizophrenia is a genetically determined metabolic disease entity, one characterized by alterations in the metabolic pathway for the breakdown of yet unidentified but endogenously occurring compounds. Some clinical and laboratory findings have suggested that as in other metabolic diseases, a basic deficiency may exist, in varying degrees, in different persons so affected. Recent research has emphasized a possible role of neurohumoral amines in mental health and disease, particularly nerepinephrine, serotenin, tryptamine, and histamine. It has not been possible thus far, however, to measure the presence of such agents in the normal or schizophrenic human brain during life, as has been done with animals, and so to link them conclusively with behavioral states.

Still other investigators have explored urinary aromatic substances in schizophrenic patients, more particularly as to the presence of abnormal indoles. Underlying this approach has been the thesis that if a chemical or viochemical alteration should be related to a disease in some way, it should be reflected in the chemistry of the urine. Again, however, methodological difficulties have hampered this research—many organic substances in the urine are still unidentified; others are present in such minute quantities as to be unidentifiable; many metabolites are also extremely unstable and undergo changes within the urine. Thus far no metabolite has been dentified as conclusively characterizing the urine of schizophrenic patients.

ith the greater refinement of instrumentation and the development of ultramichrochemical procedures it may be possible one day to have available brain tissue for more reliable study of the biochemistry of schizophrenia.

Family studies, psychodynamics, and child development

Most of those investigators presently carrying out research in the biology or biochemistry of schizophrenia assume that psychosocial factors, if related at all, play a secondary role in poducing the characteristic symptoms of schizophrenia. A fast-growing body of other research investigators assign primary responsibility to family developmental factors in the production of schizophrenia. Few investigators are professionally equipped today to carry out research in both areas, thus making difficult the achievement of that much-needed overall framework in which to concepualize schizophrenia.

Increasing numbers of research workers are exploring what might be termed a psychogenic theory of schizophrenia—many thorugh studies of the family interaction of schizophrenic patients. Among some of these studies currently supported in the Insitute research grant program are research on attitudes of relatives of mental patients, on family interaction and psychopathology in schizophrenia, on social and individual systems in schizophrenia and on competitive and cooperative social interaction. Other studies are inquiring into developmental processes in childhood schizophrenia, on language development in childhood schizophrenia, followup studies of infantile autism, and explorations into symbiotics child psychosis.

The problem of diagnosis and the need for improved diagnostic methods is particularly crucial in the study of childhood mental disorder. One Insitute-supported investigator, studying autism in childhood or the problems of children whose worlds are governed by personal needs and wishes at the expense of objective reality, has recently emphasized the need for clarification of the differential concepts of childhood schizophrenia. A close, but not invariant, relationship exists between the symptom of autism and the nosological classification of childhood schizophrenia. Some children may manifest autistic isolation and autistic thinking yet not be psychotic; others may be both.

Beneath the continuing descriptive studies of family dynamics and childhood schizophrenia is the search for the source of the syndrome. During 1960 one group of Yale University investigators, supported by a long-term Institute research grant reexamined the findings of their 7-year project. These investigators recognize that their research cannot settle questions of causation and do not exclude organic determinants which may impinge on the learning process. Nevertheless their detailed study of 20 families of young schizophrenic patients found no family which functioned or had ever functioned in a way which could be characterized as wholesome, normal, or as falling within the usual range of family life. These investigators list a variety of characteristic forms of family dysfunction which they believe are related to schizophrenic manifestations.

Although evidence is accumulating on abnormal interaction and organization which often exist in families of schizophrenic patients, no definite proof has yet been offered which would assume such family background to be a directly attributable cause of mental illness.

Other studies related to schizophrenia

In addition to the research areas discussed above, a variety of Institute studies of cross-cultural problems of mental illness and of the epidemiology of schizophenia are also contributing to our knowledge of this disorder. Psychological research in perception and cognitive study also has much to contribute. Among some of the many current grant-supported projects are included studies of the mechanisms of perception and personality relationships, studies of time sense in normal and psychopathologic states, studies of patterns of thinking in psychiatric disease, experimental study of schizophrenic thinking, and the study of the nature of symbol formation and its role in cognition. Psychometric research is still another fruitful area in application to the study of schizophrenia.

THE INTRAMURAL RESEARCH PROGRAM

As has been noted earlier, the disturbances in schizophrenia are so pervasive and so numerous that many lines of investigation, even those with a central focus in areas other than purely psychiatric, are being carried on in the intramural research program. For example, current studies of developmental processes, both normal and pathological, have significance for research in schizophrenia. In what manner does the human organism develop? What is the impact of early experience and environment on its development? What are the effects of parental attitudes and practices on this process? What are its modes of adapating to its environment? What are the factors that make for normal development on the one hand and pathological development on the other? The answers to these questions may provide investigators with some of the pieces they need to gain an understanding of the etiology, prevention, and treatment of schizophrenia.

Many other ongoing projects in the intramural program fall into a similar category; i.e., they are not concerned directly with schizophrenic processes but are basic to any understanding of both mental health and mental illness. Among these are psychological studies of human and animal behavior, sociological studies of various conditions which seem to set the stage for the onset and development of pathological behavior, and studies of stress and adaptation. Studies of the biochemistry, pharmacology, and metabolic processes of the central nervous system and the electrical activity of the brain and their relation to behavior can also help to elucidate the problems of this group of mental disorders. The intramural research program has considered it of the utmost importance that all relevant theories of the etiology and pathogenesis of schizophrenia be investigated—those which emphasize biological factors, as well as those which place stress on the social and psychological aspects of behavior.

How does the behavior of the schizophrenic patient differ from that of normal individuals? Evidence seems to indicate that the cognitive processes of the schizophrenic are impaired. If so, what is the nature of this impairment? A number of current studies aim at developing precise methods for measuring various mental and motor functions of schizophrenic and normal populations to discover the nature and extent of existing differences.

Another group of workers is investigating the role of heredity in schizophrenia, specifically, the relative contributions of heredity and life experiences to the severity and forms of expression of schizophrenia. Their work indicates that there is a group of schizophrenics in which heredity may play an important part. In male patients in this group the form of the illness is mainly a severe catatonia. Another group of schizophrenics exists in which heredity seems of minimal or no importance. In males in this group the form of the illness is mainly paranoid and is relatively mild in that the onset is late and the outcome nondeteriorating. The major studies in the field of family relationships tend to support the theory that psychological influences play a significant role in the manifestations of schizophrenia.

Treatment processes in schizophrenia are being studied in the intramural program concomitantly with investigations of the environment or social structure of the setting in which therapy takes place. Social scientists and their colleagues in psychology and psychiatry, well aware that mental patients' contact with nurses and aids may have important bearing on the course and outcome of illness, are studying factors which influence the attitudes and behavior of the therapeutic personnel.

Work on family relations in schizophrenia continues. The Institute's clinical research program is attempting to define more precisely the dynamics of family interaction in the schizophrenic as contrasted with the nonschizophrenic family. The schizophrenic offspring seems to play a different family role and has different familial experience than his nonschizophrenic siblings. One investigator has had remarkable success in predicting from psychologcal tests of family members, which families have a schizophrenic member; when given the results of the patients' tests, she has succeeded in matching the patient with his family. She was able to do this when she concentrated on the form of the thinking rather than the content, e.g., the way in which attention and meaning were manipulated. Investigators in this project are engaged in family rather than individual therapy and find it a useful device for illuminating certain unique aspects of behavior and uncovering significant relationships within the family constellation which are not revealed in the more conventional therapeutic approaches.

A current hypothesis relating to the pathogenesis of schizophrenia has postulated a defect in the metabolism of epinephrine in this disorder with the production of certain abnormal derivatives which in turn may account for the major symptoms of the disease. This hypothesis was developed at a time when the knowledge of normal metabolism of epinephrine was extremely vague and it was possible to account for only a small amount of the epinephrine released in the body, this being the epinephrine which was not altered by body metabolism but was excreted in the urine unchanged. In order to test this hypothesis in schizophrenia, it was first necessary to learn the normal pathways of metabolism. Studies by Institute scientists of normal animals and man extending over the past several years have now made it possible to account for practically all epinephrine administered and also that presumably produced in the body in the form of two major metabolites, metanephrine and 3-methoxy-4-hydroxymandelic acid, and four minor metabolites including unchanged epinephrine. Based upon this work other investigators in the past year have completed a definitive study of the metabolism of circulating epinephrine in a group of schizophrenic patients. The findings from this study argue against the presence of a major abnormality in the metabolism of circulating epinephrine in this disorder.

One of the most interesting aspects of modern neurochemistry has been the finding that a number of amines with rather potent pharmacologic effects elsewhere in the body are differentially localized in various parts of the brain. These include among others norepinephrine, serotonin, tryptamine, and histamine. The distribution of these substances in certain functional areas of the brain and the alterations in their concentrations which occur in association with the action of potent psychotropic drugs such as reserpine or iproniazid, have suggested that these agents may play an important role in normal behavior and may be implicated in schizophrenia. Although the synthesis, destruction, and levels of these compounds in the brain can and have been measured in animals and correlated with behavioral state, no such direct approach is possible in man for ascertaining the possible role of these substances in mental states or in the highly specialized behavioral patterns of normal and schizophrenic human beings. Studies in the blood or urine may serve to detect general abnormalities in the metabolism of these agents if they occur but are not sufficiently sensitive to elucidate their specialized metabolism in the brain. An ingenious technique based upon double-labeling has been devised by an Institute scientist which theoretically appears capable of yielding information on the brain metabolism of biogenic amines from studies of blood and urine, but numerous methodological problems remain to be solved before it can be applied to man.

One of the important accompaniments of human stress is the release from the adrenal gland and the sympathetic nervous system of the important hormones, epinephrine and norepinephrine. The available techniques for measurement of the amount of such release and its correlation with other measures of stress in health and disease have been quite unsatisfactory, depending as they do upon analysis of the urine for epinephrine or norepinephrine which are excreted unchanged. Since more than 95 percent of these hormones are converted to other substances before excretion, any attempt to estimate the amount secreted from an analysis of this extremely small residue is associated with the error which may be several hundred percent in magnitude. On the basis of new knowledge concerning their metabolic pathways, new degradation products of these catecholamines have now been identified. In the past year workers have developed a technique for the determination of 3-methoxy-4-hydroxymandelic acid (VMA) in the urine of man. Since this compound in the urine accounts for some 40 percent of both injected and presumably endogenously produced epinephrine, it is a much closer indicator of catecholamine secretion in various states, and has provided a more reliable method for measuring responses to stress.

TRAINING

The Institute's support for the training of professional personnel in skills relevant to schizophrenia is maintained as an integral part of the training grant program in psychiatry, psychology, biological and social sciences, social work, and nursing. In addition, a large share of the Institute fellowship program supports the training of scientists in research skills associated with the understanding and treatment of schizophrenia.

BIOMETRICS PROGRAMS

As part of its total program, the Biometrics Branch is engaged in measurements of the prevalence and incidence of mental disorders, and relating this information to pertinent factors of demography, sociocultural environment, and treatment programs. In conjunction with this function, the Institute's biometrics program provides consultative and direct services to State and local departments of mental health. The Branch also supports a long-range program to improve and coordinate the flow of statistical data from various sources in the United States.

The expansion of the newer treatment methods, such as day, night, and open hospitals as well as psychopharmacology, has led to increased complexities in the interpretation of statistical data, and has emphasized the need for new statistical reporting systems of adequate scope and flexibility. A model reporting area, in which mental health statistics are processed each month, now includes 22 States. Cohort studies of the fate of schizophrenic admissions (among others) have shown wide interstate variations in release, retention, and death rates, as a function of hospital policies. A refinement of a cohort study is now attempting to control some of the variables which contaminate the comparability of the data.

Through the national reporting program on outpatient psychiatric clinics, data are also available on services to schizophrenic outpatients. Approximately 3,000 children and 15,000 adults discharged from 1,001 reporting clinics in 1959 (70 percent of the 1,429 clinics in the country) were classified with a schizophrenic reaction. This represents only 5 percent of the child patients but about one-fifth of the adult patients diagnosed with a mental disorder. In a comprehensive study in Maryland for 1959 conducted by the Institute, it was possible to compute rates of discharge from clinics per 100,000 population.

Not only are biometric data of importance in sensing the distribution and flow of types of mental disorder under various conditions, but it is probable that comparative data will further the refinement and standardization of present-day clinical diagnostic data.

COMMUNITY SERVICES

The responsibilities of the Institute's Community Services Branch include efforts to improve, extend, and strengthen State and local programs for the care, treatment, and rehabilitation of the mentally ill. Professional and technical assistance to State and local programs is provided through staff of the National Institute of Mental Health in headquarters and in eight regional offices. Special staff is available for hospital consultation, group consultative studies, and surveys. The consultation which is provided covers the full range of services for the mentally ill, including services in clinics and general hospitals, mental hospitals, alternatives to hospitalizaton, and aftercare and rehabilitation in the community.

The growing trend to experiment with the new methods of care and treatment, and to decentralize and develop new services for the mentally ill in the local community, make it especially important that consultation be available at this time to disseminate the most recent knowledge from research, from pilot projects, and program experience. While consultation is not usually centered only on schizophrenic patients, as has been indicated previously, schizophrenic patients represent a large proportion of the mentally ill in hospitals and in communities.

Besides administering the mental health project grant program, which is focused on the mentally ill, the Community Services Branch is also responsible for the Federal program of grants to States for community mental health services. The Community Services Branch, since 1955, has utilized technical assistance projects to extend consultation and grant-in-aid services to State mental health authorities. Ten technical assistance projects have been concerned with followup services to psychiatric patients upon their return to the community—in Kentucky, Iowa, California, Pennsylvania, Massachusetts, Maryland, North Dakota, Nebraska and Missouri. These projects have brought together community and State leaders to determine which services existed and which services should be implemented to aid in the patients' integration into the community. These exchanges of information are reflected in the extension of community health programs in both preadmission, halfway houses, hospitalization of psychiatric patients in local general hospitals, and in a marked increase in aftercare services provided to psychiatric patients returning from State hospitals. Twenty-three States have specifically delegated State staff time to extend the development of these services. These same efforts have also resulted in five State staffs beginning a new phase of work with volunteers. These efforts have been to aid the volunteer to assist the psychiatric patient in his development, extension, and maintenance of social relationships both within the institution and in the community.

Applications for mental health project grants have continued to increase, not only in terms of the number of projects and amount of funds expended, but in the scope of coverage in terms of areas of investigation and increased geographic distribution.

Three basic approaches have been emphasized in this program: (1) improved hospital care and treatment; (2) improved administrative practices, and (3) improved community mental health programs. Special consideration has been given in this program to projects related to schizophrenia, more particularly new methods of patient care, preadmission services and followup services. Studies of followup services constitute the largest number of grants in the mental health project grant program.

Among some of the current demonstration studies of new or improved methods of care are a pilot day nursery school for schizophrenic children, a group psychotherapy program for Puerto Rican schizophrenic patients, projects utilizing family-centered treatment of schizophrenia, studies on role relations and rehabilitation of schizophrenic patients, symposia on treatment methods in schizophrenia, the study and demonstration of aftercare services for psychiatric patients, and the study of treatment alternatives to psychiatric hospitalization.

MENTAL HEALTH PROJECT GRANTS

The program of mental health project grants established by title V, Public Law 84–911, is designed to provide support for investigations, experiments, demonstrations, studies, and research projects with respect to the development of improved methods of diagnosing mental illness, and of care, treatment, and rehabilitation of the mentally ill. The program includes grants to agencies responsible for the administration of State institutions for the mentally ill for developing and establishing improved methods of operation and administration of such institutions. Mental health project grants program was established for the purpose of encouraging hospitals and community agencies to experiment with projects to increase knowledge concerning mental illness and its treatment, and to find more effective ways to utilize the knowledge acquired. There is an acute need to move programs which are service oriented in order to stimulate new methods of treatment and to find more effective ways to use personnel and facilities. Projects are currently focused on methods of prevention, techniques of early identification, development of services to treat in the community those for which such treatment is indicated, improved treatment for those hospitalized, and more effective programs in the community and hospital to effect the early return of patients to the community. Among the projects requesting support special emphasis has been directed toward those pertaining to critical areas such as alcoholism, aging, juvenile delinquency, school mental health, mental retardation, and schizophrenia. During the 3 years of operations of the program of mental health project grants there has been an increasing volume of applications requesting support for projects covering a wide range of approaches to a variety of problems.

ALCOHOLISM

The problem of alcoholism extends to large numbers of persons in the population and has a direct effect on the families of the alcoholics, on industry, on allied welfare services, and on programs of medical care. The alcoholic frequently is reluctant to accept treatment and the general practitioner, the community clinic, and the general hospital often are not interested in providing services to him. Illustrative of the projects being supported in this area is a study in which psychiatric personnel are available in the emergency treatment room at the hospital to establish immediate contact with patents requesting any type of emergency service but for whom alcoholism is a significant part of the problem presented. Prior to this experiment patients were referred to the alcoholic clinic but seldom followed through with appointments. Early results of the study indicate that over 40 percent of the patients contacted by the psychiatric personnel in the emergency room have continued treatment as compared with approximately 2 percent of the control group referred to the clinic through regular procedures.

In the Midwest a project is being supported to provide a training course for physicians. This project is designed to determine procedures that may enable the general practitioner to be more effective in the treatment of alcoholic patients. The physicians are provided with a 4-week training course. Bimonthly seminars are conducted through a tele-communication system and visits are made to the physicians on a monthly basis by a psychiatrist and a nurse. This project is demonstrating that the general practitioner can be more effective in the treatment of alcoholic patients.

Another project in the area of alcoholism is being conducted on the orientation of wives toward their husbands' alcoholism. It is focused on increasing knowledge concerning family adjustment to stress situations by exploring some of the variables concerned with socioeconomic background, marital roles, and how the married couples view alcoholism.

AGING

The number of aging persons in the population of mental hospitals and the feasibility of retaining many of these individuals in the general community has been a problem of increasing concern. A study of the patients in a representative State hospital is being conducted to determine the number of patients who might be there for geriatric reasons rather than psychiatric illness and is comparing this group with geriatric patients handled by other types of institutions and social agencies. On the west coast a project is studying the social rehabilitation potentials of geriatric patients in a State hospital in order to evaluate the services needed in the community to provide adequate resources for those patients who might be released if such services were available. In the Midwest a project is exploring the use of productive and remunerative work in a rehabilitation workshop setting as a technique for arresting, retarding, or reversing the process of psychological aging; this project is designed to encourage older persons to remain in the community after having applied for admission to a home for the aged.

JUVENILE DELINQUENCY

During 1961, as a result of the increased appropriations made available by the Congress, there has been a significant expansion of the mental health project grants program in the area of juvenile delinquency. One project is designed to test intervention into the lives of hostile children who do not participate in social group experiences. This is an effort to reverse an aggressive behavior pattern after it has developed to the point where the child's conduct has brought him into conflict with the school and community. Another project is experimenting with a unique method of treating delinquent children by forming therapy groups within the institution prior to the time of return to the community and then continuing to work with the same group after the individuals are discharged into appropriate individual living situations.

Studies are exploring possible alternatives to institutional placement in those cases where it appears necessary to remove a child from the home or community. Other studies involve the rehabilitation process and evaluation of various means of easing the transition from the institution to the community on release of the offender. Among these are such methods as "halfway houses" and continued therapy in a group formed within the institution and released as a unit. A number of studies include research on modifications of treatment within institutions, such as changes in the structure of treatment groups. Also, there are studies of institutional treatment with special populations, such as withdrawn or aggressive children. Other studies are concerned with the inmate culture of the institution, including staff and clients, and the relation between the inmate culture and the goals of the organization. Special problems may arise when a treatment orientation is introduced into an institution which has previously been primarily custodial. Methods of dealing with these problems are being evaluated.

Of special importance in the field of juvenile delinquency are long-term followup studies as the relationship between delinquent development and the achievement of adult roles needs careful examination.

MENTAL RETARDATION

In the Midwest a project is demonstrating the effectiveness of a comprehensive diagnostic service for children who are being considered for institutionalization. Counseling services are offered to parents. This project also offers training opportunities for physicians, psychologists, social workers, and teachers. Information regarding methods of diagnosing and treating mentally retarded children is being introduced into the curriculum of the medical school.

The program of mental health project grants provides a flexible mechanism for research, experimentation, and demonstration of a wide variety of techniques. In the Southwest there is an ongoing project designed to provide a method of introducing mental health services in rural areas. Consultation is made continually accessible to local communities by a professional mental health specialist living in the community, who endeavors to stimulate community interest in a comprehensive approach to mental health services and needs and acts as a liaison with existing services throughout the State. Another project is demonstrating the effectiveness of family care for released mental patients in foster homes. On the west coast a State medical association is involving general practitioners in the aftercare of discharged patients from mental hospitals by providing orientation case conferences prior to discharge and making available continued psychiatric consultation. The Academy of General Practice grants educational credit to participating physicians and there is extensive involvement to the department of psychiatry at the State university.

The past year has been one of growth, progress, and accomplishment for the program of mental health project grants. The increase in number, variety, and quality of requests for support indicates that this program can be profitably extended to help meet more effectively the acute need of the field of mental health for improved methods of care, treatment, and rehabilitation as well as new methods of prevention of mental illness and the promotion of mental health.

CLINICAL NEUROPHARMACOLOGY RESEARCH CENTER

The past year has seen a further development of the collaborative program between the Clinical Neuropharmacology Research Center (CNRC) of the National Institute of Mental Health, and St. Elizabeths Hospital. This program, which comprises both laboratory and clinical facilities was initiated to provide close interaction between laboratory scientists and clinicians in a typical mental hospital setting. The center is making its steady contribution to problems of overall planning within the hospital, to research in the laboratory and clinical areas, and to the training of psychiatrists in research method, and in neuropharmacology. It has become an important part of the intellectual life of St. Elizabeths Hospital and the National Institute of Mental Health.

CLINICAL STUDIES

As hitherto, the clinical studies have centered on problems in the care and treatment (including the pharmacotherapies), of the chronic schizophrenic patient, a numerically preponderant problem in State institutions. A comparative drug study involving two tranquilizers (prochlorperazine and trifluoperazine) and a placebo was initiated to examine in some detail and with special emphasis on sources of error, the effects of nondrug factors known to affect the response to medication in a typical mental hospital setting. Essentially, the study thus aimed at (1) determining the effect of physical environment on the responsiveness to drugs; (2) determining the effect of various types of nursing care and, particularly, nursing in small groups, on drug response; (3) the cultivation of native therapeutic and research skills often found, but ignored, in ward personnel; (4) the codification of a number of questions commonly entering into a drug trial in a mental hospital setting (i.e., the selection of patients, selection of drugs, selection of experimental design, the technique of drug administration in a blind study, the assessment of side effects, management of adequate laboratory control, and the comparison of a number of clinical evaluative techniques); (5) the monitoring of attitudes toward research; and (6) the institution of data reduction techniques suited to a drug study conducted in this manner. The dimension of the study was kept within the limits of applicability and feasibility in a mental hospital setting, so as to encourage a retesting of the conclusions in other services of St. Elizabeths Hospital and other State institutions. An analysis of the data, though not yet complete, has pointed to several sources of error in assessment. Some positive and empirical trends, however, are equally apparent. A coordinated program of clinical investigation, proceeding simultaneously in a number of wards of a mental hospital building (rather than a single "research service") can profoundly, and with great economy, contribute to the increasing of both therapeutic and research skills of personnel throughout such a building. The systematic review of methods and of data can become an instrument for education of personnel. Nursing in small groups, structured around the skills of attendants and of relatively intact patients, can act as a pacemaker in decisively changing the therapeutic climate of a chronic ward. Such a program, while contributing to the rehabilitation of patients, reduces the consumption of tranquilizers on a ward; it also changes attitudes of personnel. The measurement of patient behavior by way of rating scales, while having its limited use, also has serious drawbacks. Some documents furnish much higher interrated reliability than others, and some are more sensitive to fluctuations in the clinical picture over time than others. Equally important is the measurement, in an objective manner, of the amount and pattern of social interaction between patients within a ward. An instrument for this purpose has been developed by a CNRC scientist and has been found useful and sensitive in quantifying changes brought about by psychoactive drugs, and group nursing techniques. It has also given an indication of the influence of social setting on the fluctuation of symptoms in the individual patient. The instrument is to be employed in the multihospital drug study initiated by the Phychopharmacology Service Center, NIMH.

A number of other clinical studies are also proceeding. These include studies on disturbances of the attention process in schizophrenia; the possible relation between the degree of hallucination, and the quantity of dreaming, as monitored by changes in the electrical activity of the brain; and the altered ability of the schizophrenic to abstract meaning from written materials. These studies are being linked to others proceeding at the Clinical Center.

NEUROCHEMICAL STUDIES

The mode of action of drugs inducing transient mental changes in man (the so-called psychotomimetic agents) is of great theoretical and applied interest. The theoretical interest derives from the need to understand the chemical changes undergone by a drug in the body, and the effects of the compound, or its metabolic products on the brain. The applied interest rests in the hope of antagonizing the effects of a drug through a biochemically related compound. A new type of psychotomimetic compound is being studied at present both in the laboratory and the wards. The interest of this group of drugs (dimethyl and diethyltryptamine) lies in their close chemical relation to indolic compounds (serotonin and cognate substances) known to occur naturally in the animal body, and the brain. Studies have now given strong indication of the endogenous conversion of the drug into a more active derivative (6-hydroxy diethyltryptamine) in the animal body. This finding provides one of the very few known instances of the metabolic conversion of a psychotomimetic compound into a more active derivative within the body. Furthermore, joint studies with a behavioral scientist at center have shown that the rate of this conversion differs from animal to animal in the same species (rat) ; and that this difference in rate corresponds to differences in behavioral threshold for the parent substance. The higher the rate of biotransformation to the 6-hydroxy derivative, the less of the parent substance was required to produce a given behavioral effect in a particular animal. These findings thus provide a sound experimental setting for combining behavioral (operant conditioning) techniques with metabolic exploration in the individual animal. They stress interindividual differences in the metabolic handling of a particular compound in members of the same species, and derive their theoretical importance from the aforementioned chemical relation to natural tryptamine derivatives.

The occurrence of catecholamines in certain parts of the brain and the concentration changes observed in some conditions, including drug-induced states, suggest a connection of brain catecholamines with brain function. Studies by Institute scientists, and others, have centered on the distribution of these highly active biogenic amines within the nerve cell. It could be shown that the amines may be separated into two broad fractions, the first present in the cell sap, and the second concentrated in minute granular matter inside the cell. According to current concepts, the former is biologically active, while the latter may serve as a store. The effects of reserpine, phenylisopropylhydrazine (an energizer of the monoamine oxidase inhibitor family of compounds), and a number of other drugs have been examined alone, and in combination with each other. Particular attention was paid to the intracellular redistribution of catecholamines in the two fractions brought about by these drugs. The findings have emphasized the importance of intracellular economy in an appraisal of the mode of action of psychotropic drugs, and may necessitate a reexamination of current theories concerning the mode of action of reserpine and related compounds.

A number of hormones, including the sex hormones, are known to affect behavior, although mode of action on the brain is far from clear. In an attempt to analyze the effects of hormones on cerebral mechanisms, an Institute visiting scientist has developed a method by which a small amount of solid hormone can be implanted directly into the brain of cats. As reported last year, it was shown that the implantation of hormone into the posterior hypothalamus markedly altered the sexual behavior of such animals. The distribution of the hormone locally in the brain has now been studied, using radioactive C–14 labeled hormone. Results suggest that a small and highly localized area of the brain immediately adjacent to the site of the implant is subjected to a prolonged, steep concentration gradient of the hormone; and, also, that some cells in the hypothalamus may be selectively sensitive to the action of sex hormones. The peculiarity of this region is also borne out by the finding, on the part of our scientists of the relative freedom with which norepinephrine and epinephrine enter the hypothalamus, compared with other areas of the brain. The importance of regional economy within the brain is borne out by these and cognate observations.

Whereas it is convenient to study the action of drugs on the brain by direct intervention, it is equally important to establish reliable methods for monitoring chemical changes in body fluids which, albeit indirectly, may reflect changes within the brain. A number of such methods are being developed by Institute scientists for the estimation of most of the catecholamines, and their metabolites, in blood and urine. Similarly, methods for the estimation of metabolites of diethyltryptamine have been developed to a degree which makes possible their use in metabolic studies in man. Lastly, a long-term study is proceeding, aiming at the identification of the principal metabolic products of chlorpromazine in the experimental animal and in man. The success of this study will depend upon the availability of reference compounds of known chemical constitution.

ELECTROPHYSIOLOGICAL STUDIES

The psychoactive drugs are known to exert marked effects on autonomic functions such as blood pressure, temperature regulation, and respiration. The cell aggregates situation in the midline region of the brain stem which govern some of these vital functions (such as respiration) are characterized by rhythmic electrical discharge. Little is known at present concerning the mechanisms underlying this rhythmicity. In an attempt to elucidate this property, Institute scientists have examined the patterns of electrical discharge obtained from single cells mediating respiratory activity. Using microelectrodes and micropipette techniques, records have been obtained from the outside and from the inside of single respiratory cells. The latter represent the first intracellular recordings obtained from neurones in the lower brain stem. The results have defined three separate factors which produce rhythmic discharge of the respiratory neurones, and furnish a foundation upon which further pharmacological inquiry can be built.

A similar program is now proceeding to localize the patterns of electrical discharge of cells in the brain stem controlling blood pressure, and to analyze the mechanisms affecting the repetitive discharge of these neurones. These physiological data will be used in a detailed analysis of the effect of drugs (applied both locally and systemically) upon the central steering mechanisms governing blood pressure.

Another study is centered on the so-called direct current (d.c.) changes on the surface of the cerebral cortex. The occurrence of such changes, following sensory stimulation, has been variously reported and denied. Using a compact, sensitive electrode of special construction, an Institute scientist has developed a method for recording these phenomena in the lightly anesthetized and conscious animal. It could be shown that these d.c. changes are highly sensitive to experimental conditions; but, that with proper care, they can be regularly obtained even in the conscious animal. The characteristics of these changes have been defined. The response to auditory stimulation in various areas of the brain has been studied. The method represents a definite technical advance in the study of direct current changes on the surface of the brain. Their relation to the processes of attention, sensory discrimination, and the effects of drugs influencing sensory function will be further examined.

In sum, then, the clinical activities of the Clinical Neuropharmacology Research Center have been expended in creating within the wards of the Center a standard of care and observation which will serve as a necessary prerequisite for the more detailed studies which are now being initiated. Special attention has been paid to the interaction between the social-therapeutic measures, and the drug therapies in the management and treatment of the chronic schizophrenic patient. Methods are being developed to study these complex interactions in a quantitative way. The therapeutic program has been markedly successful in acting as a pacemaker for other services of the hospital. It will be linked to day hospital and follow-up facilities, as and when they develop.

The laboratory program has centered on problems concerning the mode of action of drugs on the brain, with special reference to aspects of regional distribution and economy within the brain. The location of this program within Saint Elizabeths Hospital has furnished the Institute scientists with a constant and growing opportunity to interact with their clinical colleagues, and has provided a link both scientific and human, between the laboratories and services of the Clinical Center, Bethesda, and Saint Elizabeths Hospital.

STATE CONTROL PROGRAMS IN MENTAL HEALTH

Mental health grant-in-aid to States is designed to assist the States in establishing, extending, and strengthening mental health services, and to help in the development of statewide mental health programs of community services. The goal is to develop high-quality, comprehensive, coordinated programs for the promotion of mental health, the prevention of mental disorders and the improved diagnosis, care, treatment and rehabilitation of the mentally ill.

Staff at the National Institute of Mental Health, inclusive of the Regional Offices, is in a unique position to observe and evaluate developments throughout the Nation. From this vantage point of overview, a major role is performed by the staff through the use of several devices and techniques in working with State and local personnel. Among the services performed are those of the identification of gap areas in services and programs, the evaluation of the existing programs and activities, the exchange of information and the stimulation of new approaches in the States and local communities to the amelioration or solution of existing and emerging problem areas. These activities are undertaken in partnership with National, State, and local official agencies in cooperation with voluntary and private agencies and individuals.

NEW CONCEPTS IN MENTAL HEALTH

New mental health concepts and methods stress continuity of care beginning in the community with programs designed to provide appropriate treatment for patients in the community when this is feasible, such as outpatient services, emergency care, foster-home placement, day and night hospitals, and increased use of general hospitals for the treatment of psychiatric patients.

In cases where hospitalization is indicated, new methods are being tried such as open wards, therapeutic communities, patients' clubs, and a variety of other treatment techniques which tend to result in shortened periods of hospital care.

When patients return to the community a variety of facilities are essential to provide adequate follow-up care, such as clinical services, foster homes, half-way houses, vocational rehabilitation training and placement, nursing care, family counseling and other activities. An adequate program includes a wide spectrum of services both community-based and hospital-oriented which must be integrated into a pattern that provides continuity of care for the appropriate treatment of the individual depending upon his particular needs.

ROLE OF NIMH STAFF

In their work with State and local programs, Institute staff encourage innovation, identify gap areas, and stimulate the trying out of new methods and techniques and the evaluation of both the old and the new approaches and procedures. In the partnership of "research and development" the emphasis through professional and technical assistance is upon "development."

Through its professional and technical assistance staff, and particularly through the regional mental health staff, it is possible for the National Institute of Mental Health to reach every community in the Nation and maintain a communication network for the widespread dissemination of knowledge as it becomes available from basic and operational research.

Staff provides the consultation required to translate research findings into the everyday practice of an operating program; and from continuous contacts with ongoing State and local programs, technical assistance staff provide feedback to the Institute on needs, problems, and areas requiring development in the research and training activities of the Institute.

THE FEDERAL SHARE

Through State control programs and other means revolutionary progress has been made in mental health programs in the last decade.

Federal grants-in-aid to States for mental health activities increased from $4 million in 1959 to $5 million in 1960, and to $6 million in 1961. These funds were used for the promotion of mental health and the prevention of mental illness, and for other community services for the improved diagnosis, treatment and rehabilitation of the mentally disturbed, exclusive of inpatient care in hospitals and institutions. The increased allocation enabled the minimum grant to States to be increased from $25,000 in 1959 to $40,000 beginning in 1960.

While on an individual State basis these funds appear to be small, their impact on State and local areas has been significant, and as the funds have increased Institute staff has been enabled to stimulate an increasing range of activities.

Major increases have occurred in State appropriations, in the number of community clinics, psychiatric units in general hospitals, day and night hospitals, after-care, and rehabilitation services. The number of patients in State mental hospitals has decreased and more responsibility for the care and treatment of the mentally ill is being carried by local communities. Community mental health laws providing for continuing State grants to locally administered programs have been enacted in a significant number of the States. State support of pilot projects, demonstrations, training and research has been expanded.

In other respects Institute staff also have been instrumental in effecting changes in a number of areas which present both health and social problems, e.g., aging, alcoholism, drug addiction, juvenile delinquency and mental retardation.

In addition to the administration of the mental health project grants program and the technical direction of the program of Federal grants to States for community mental health services, and consultation, staff are engaged in a wide range of other activities including State surveys, inservice training, field demonstrations and pilot projects, program analysis, and operational studies.

An effective means of extending both preventive and therapeutic mental health services is through the device of mental health consultation to numerous State agencies and to local communities regarding the incorporation of mental health concepts into their program. Mental health education of the general public also continues to be a major activity. Pilot projects, evaluative studies and training activities have been endeavors begun with Federal funds; and after such time as has been necessary to demonstrate their value, the State and local governments have assumed their support.

TECHNICAL ASSISTANCE PROJECTS

Technical assistance projects, developed during the past 6 years, are a method of providing consultation, stimulating new approaches, and the affording of technical assistance to States. In these projects, national experts meet with State staff in an institute or workshop focused on a specific mental health problem. In addition to being educational in nature, these projects are used to explore needs and resources in new program areas, plan and develop methods of meeting these needs through stimulation of the development of new services, and to facilitate coordination among State agencies.

Technical assistance projects have a national impact as reports of the projects are published, and are distributed and discussed widely. In 1960, 27 projects were completed, covering a wide range of subjects including psychiatric units in general hospitals, public health nursing services, clinics, aging, alcoholism, delinquency, and school mental health.

PROGRAM DEVELOPMENTS AND APPROACHES

It is recognized, of course, that mental health programs cut across many areas of interpersonal relationship which do not lend themselves to communication through traditional public health channels. In this context consultation by Institute staff should be provided to schools, welfare agencies, correctional agencies, family service agencies, and many other community resources whose programs provide access to constructive work with people in need of help. Each of these services provides research settings and experience in the development of sound mental health concepts.

The stimulation to States resulting from grants-in-aid to the States in conjunction with the consultation and the Mental Health Project Grants program (title V, Public Law 911, 84th Cong.) has been a decisive force in effecting changes reflective of the newer concepts in the prevention, treatment, and rehabilitation of the mentally ill.

FUTURE NEEDS

Program planning indicates the following areas for future support:

(*a*) Expansion of activities concerned with the promotion of mental health and the prevention of mental illness through work with nonpsychiatric agencies and groups such as schools, health and welfare agencies, general practitioners, etc.

(*b*) Aid in the accelerated development of community services such as outpatient clinics, psychiatric wards in general hospitals, and improved techniques for followup care for ex-mental patients.

(*c*) Improvement of care, treatment, and administration in mental hospitals, through stepped-up emphasis of concepts of treatment rather than custody, and through "open hospitals," "therapeutic community," improved hospital-community relationships, and new treatment methods.

(*d*) Experimentation with administrative patterns for providing mental health services in rural and sparsely populated areas which are now without services.

(*e*) Development of services in the special areas such as aging, alcoholism, drug addiction, juvenile delinquency, and mental retardation.

(*f*) Encouragement, through pilot projects and demonstrations of the development of the "growing edge" in State and local programs in the trying out of new methods and techniques.

(*g*) Experimentation with new ways of the more effective use of existing mental health staff in mental-health programs and possible ways of using new types of personnel.

(*h*) Expansion of State and local programs of training and research activities.

(*i*) Development at the State and local level of long-range planning and coordination of mental health services.

Mr. FOGARTY. Before I close, I just want to say I don't think it is your fault, Doctor, because you asked for more money; but I for one am very disappointed with the budget that you have come up with. It is not very forwardlooking, in my opinion. I don't think it will allow for much progress unless we do something about it, unless we give you more money.

Mr. DENTON?

RESEARCH ON BARBITURATES

Mr. DENTON. In your work on drugs, do you do anything about barbiturates?

Dr. FELIX. We are studying those at Lexington at our Addiction Research Center. We are studying this in two ways. We are studying barbiturates in relationship to narcotics and we are studying barbiturates in relationship to the so-called tranquilizing drugs—both ways.

Also we are studying barbiturates in relation to some of the energizing drugs. We have done a rather interesting study, Mr. Denton, studying the results of administration of amphetamine, which is a stimulating, energizing type of substance; and one of the barbiturates, seco-barbital.

We find something which I think is rather significant. If you give these substances to healthy athletes on an experimental basis, their performance will be poorer on the barbital. They think they have performed better; whereas as a matter of fact, they have not performed as well. With amphetamine, they will perform better, but they will be a little disappointed because they haven't done as well as they thought they could.

This is not to say that amphetamine is a good thing to give to a person so he can outdo himself; but the opposite of this is important for other areas. If people think they are doing better than they really are while on barbiturates, this raises a number of questions.

For instance, what about using barbiturates and driving a car? Maybe you will cut it a little too short—things of this nature. So we are going to pursue this further.

Mr. DENTON. It is like regulating the control of "bennies." Do you think there ought to be more regulation of barbiturates than we have now?

Dr. FELIX. I think the regulations at the present time are quite effective. I would concur with the recommendations of the Commissioner of Narcotics, Commissioner Anslinger, who feels, I think, he would prefer to see them under the present controls rather than more tight controls.

He is an expert in this area of controls. He is probably the world's greatest expert. If he would feel from his experience that more controls were necessary, I certainly wouldn't differ with him for a minute because I have the highest regard for his ability.

TRAINING PSYCHIATRISTS

Mr. Denton. Some years ago we set up a program to enable you to train psychiatrists. How is that program coming along? We ought to be getting results by now.

Dr. Felix. You mean the general practitioner training program?

Mr. Denton. This was right out of universities, training young students to become psychiatrists.

Dr. Felix. That program is not only, of course, to train psychiatrists, but to train other types of mental health personnel. We train social workers, nurses, psychologists, and so forth. During the time that the program has been in operation, which has been now about 13 or 14 years, there have been trained on the stipend part of this program about 10,000 different individuals who have had one or more years of training.

In addition to this, there is a number which is hard to estimate exactly who have been trained in institutions where we have had grants to strengthen the faculty, but who were not on our stipends. But I would suspect that this figure is significantly larger than the 10,000.

In addition to this, there have been grants made to almost all of the medical schools in the United States—block grants of about $25,000 each per year—to improve the psychiatric training of the medical student. So far there have been something over 50,000 doctors graduated from these schools who have been under the influence of this better psychiatric training, which makes all of them better able to take care of the psychiatric problems of their practice.

Mr. Denton. Doctor, the program shouldn't be cut back just now, do you think?

Dr. Felix. I don't propose to cut it back, Mr. Denton. The budget before you does not cut it back. It maintains it at a level figure for another year.

Mr. Denton. Do you think it could be stepped up?

Dr. Felix. Well, as I said to the chairman a moment ago, if there were no other considerations in the Federal Government for the expenditure of funds but the National Institute of Mental Health, yes, we could step it up. The potentialities are there.

Mr. Denton. There is a bad shortage of psychiatrists in mental institutions now, isn't there?

Dr. Felix. There is, yes.

THERAPEUTIC PRACTICES

Mr. Denton. I know in my hometown one of the psychiatrists told me he had 700 patients. He said, "I just can't do anything more than hit and miss with them." He said there were many cases he thought were fit subjects for psychiatric treatment if we had the psychiatrists. It would be a great saving if they had psychiatrists to take care of them.

Dr. Felix. In places where we have had adequate psychiatrists, we have found that many more patients moved out of the hospital into the community than is true in other places; plus the fact if you have such skilled people in the community in clinics and so forth, you can maintain many patients outside of a hospital who would never have to go or who could get out sooner and stay out longer.

Mr. DENTON. In that connection a number of psychiatrists have made this statement to me. They said an ordinary doctor can treat maybe 8 or 10 people in an hour, but it takes them an hour or perhaps more to treat one patient. Since they can't treat many patients in a day, they have to charge them a very high price and few people can pay that price.

So that is one factor that tends to make it less attractive, compared with other medical professions, to be doing psychiatric treatment in a community.

Have you had that problem generally?

Dr. FELIX. I wouldn't want to differ with any of my colleagues in psychiatry. But my experience has been somewhat different from this. This is my personal experience, so this does not invalidate what they have said at all.

In the first place, I have made it a practice ever since I finished my psychiatric training, to see patients. I don't charge for this service; I am a full-time employee of the Government. But I do see patients and I treat patients. I tell you this as background to what I want to say. In many cases it is not necessary in my experience to use a full hour to treat a patient. I have carried on a little project of my own for several years and I find that even in relatively long-term therapy, if I start selected patients out on a shorter period, half-hour sessions, I can do quite well.

I may not accomplish all of the ends I could accomplish with longer sessions, but I can get them back on the job, which is the first objective. That is No. 1.

No. 2, more and more we are seeing patients treated in group therapy, six or eight at a time . Some of these sessions run for an hour, some run for 30 minutes. No. 3, with the use of the new drugs, many patients can be treated by much shorter term therapy and maintained as good productive citizens on the job.

It depends on your goals. If you want to produce basic and fundamental personality changes in the patient, it may take a long time. This is a perfectly laudable, legitimate goal.

My first goal, then, in treating patients is to get them back to duty. I have found this quite rewarding. I can say, while I love my job and I have never yet seen the day—hardly any; a few once in a while—that I didn't look forward to coming to work, the best part of the day really is that part of the day when I am seeing patients.

Mr. DENTON. There is a shortage of psychiatrists, generally speaking?

Dr. FELIX. Yes, sir; this is true.

PSYCHIATRIC TRAINING OF GENERAL PRACTITIONERS

Mr. DENTON. How are you coming with your program to train ordinary practitioners in psychiatry?

Dr. FELIX. This is extremely successful. I was delighted when the Congress authorized this. But I had not, even in my own hopes and imagination, thought this would be as successful as it is. We are giving orientation courses to general practitioners so that they will be more effective in their own work, and we are also training some general practitioners to become psychiatrists.

I am not in complete agreement with some of my conferees in regard to this type of training. I think it is more important to orient the general practitioner, or the practitioners in other specialties than psychiatry, to psychiatric conditions and how to deal with them, than it is to devote too much of our energies to making psychiatrists out of other kinds of doctors. I think both approaches are important, but every doctor must understand and use psychiatric principles and techniques in his daily work with patients.

PSYCHIATRIC TRAINING OF LAWYERS

Mr. Denton. One time you talked about giving a short course in psychiatry to lawyers in law schools. Has anything been done about that?

Dr. Felix. Yes, sir; we have two such pilot projects. We will not go into this as a large program, nor do we anticipate supporting others—maybe one someplace to compare with these two ongoing projects. The first one has just about run its full course at the University of Pennsylvania School of Law. The second one is at the Yale University School of Law.

Out of both of these are to come evaluations and syllabuses which can be used in other law schools in teaching emotional aspects of the problems that the attorney meets, and phenomena of human behavior.

Some very distinguished lawyer-psychiatrists and behavioral scientists have been brought in as visiting professors for a longer or shorter period of time to teach various aspects of the course. They have tried to give them some work in counseling technique.

For instance, a couple comes in who have decided they want a divorce. They are just all fed up with each other. It may well be that with some good enlightened counseling by their attorney, a divorce won't be necessary.

It is the impression of most of the attorneys with whom I have talked that this is as much their function as it is to assist them legally to obtain the divorce. Their first responsibility is to hold the home together, if this is a possibility, they tell me.

Mr. Denton. I think that would be very valuable for a lawyer, especially in consulting with people in his office. I know when I practiced law, I think a great many people who came in to see me had mental problems more than they had legal problems.

SCHIZOPHRENIA

Some years ago you told us that you thought you might have a test for schizophrenia through a urine test, but you found out that you didn't. Often doctors have thought that in people with mental illness there was some chemical difference in their bodies or something like that. Has any further research been conducted along that line?

Dr. Felix. There is a lot of research going on along this line. Many of the leads are still open. We don't have the answers. Some have obviously been found not to be as effective as was thought and have fallen into disuse.

There is a group at the present time at the Lafayette Clinic in Detroit—Wayne University—who are studying some substances in the blood which seem to have an effect upon the ability of the red blood cells to take up oxygen. This seems to be different in schizophrenics than in nonschizophrenic normal people.

We invited one of the investigators to come to the clinical center as a guest worker for a period of time and to repeat his studies on some patients that we selected. He didn't get to see them. He did his tests blind. That is, we had some schizophrenic patients from one of the State hospitals, and we mixed these up with a group of normal people, gave him the blood, and he ran the tests, not knowing from which individuals the samples came.

He was able in a highly significant number of cases—not a hundred percent, but in a highly significant number of cases—to identify the blood of the schizophrenics from the blood of the nonschizophrenics.

Where this will go, I don't know yet. But this is one which has held up, at least through blind tests.

Mr. Denton. It would look like there was some different blood condition.

Dr. Felix. It could be. We felt for a long time—it has been a hypothesis, I should say, for a long time—that there was some relationship between ability of the brain to get oxygen and the schizophrenic condition. I remember when I was a young resident we tried giving schizophrenic patients pure oxygen in the form of inhalations to see if it would do any good. It didn't.

These investigators' studies may help us to understand why. You could get oxygen into the lungs, but you couldn't get it into the red blood cells that carry the oxygen to the place where they have to deliver it. So you weren't getting it to the place where it was needed.

Mr. Denton. Is there anything new on drugs?

Dr. Felix. There are new drugs coming out all of the time. A number of investigators over the country are evaluating these drugs on grants through our Psychopharmacology Service Center. So far, it appears as though chlorpromazine is as effective as any of them, but there are some new ones coming along.

One thing we are testing in the drugs now, because of the fact that a majority of the phenothiazine drugs—that is the group of drugs that chlorpromazine and these others belong to—caused, in doses that were effective psychologically, neurological side effects: Parkinson's syndrome—that is shaking palsy—and several other things.

It had been hypothesized that in order to get the therapeutic effect you had to push the drug to the toxic point—that is, to the point where the patient showed these side effects.

This is not peculiar to these drugs. There are other drugs in medicine which must be pushed almost to the toxic point before the therapeutic effect is achieved.

There is a drug which has been developed which doesn't have any side effects in large doses. In our nine-hospital program we are running a comparative study of the drug with the most side effects, the drug with the least side effects, and chlorpromazine as the control drug, to see if there is any difference in the therapeutic effects.

CURE RATES

Mr. DENTON. I notice in this book that Mr. Fogarty had it says that schizophrenia would cure itself in 1 case out of 5, and with treatment it could go as high as 4 outof 5. That is pretty high, isn't it?

Dr. FELIX. Yes. That is apparently the considered opinion of that group. I don't have any reason to argue with them. All of us who have treated schizophrenia have seen so-called spontaneous remissions.

So this will happen. A certain number may improve spontaneously. This is not peculiar to schizophrenia; there are many diseases in which a case now and then will get well if you don't do anything.

Mr. DENTON. I see it is 1 in 5 here.

Dr. FELIX. I don't know about the proportions. They have done some studies.

MENTAL HOSPITAL POPULATIONS

Mr. DENTON. You have clinics which are treating people as outpatients, and then hospitals treating patients. You gave us some figures about the people released from the hospital, showing that the number in hospitals had declined. When you make up your figures, do you take into account those people in ordinary hospitals, not mental hospitals, and those going to clinics? Or is that just in the mental hospitals?

Dr. FELIX. We have two sets of figures. I quoted them both. This has been going on for nearly 25 years. We receive data every year from every public mental hospital in the United States on the number of patients admitted, the number discharged, the number died, and so on. This is one group.

When I mentioned the 530,000 patients in public mental hospitals, I was talking about that group. Now we are also receiving information from a large number of the general hospitals who are also receiving patients.

Mr. DENTON. That might tend to cut the number down, though, in hospitals.

Dr. FELIX. You have to watch out here. You can do one of two things. Yes, it may cut them down for a time. But out of any given number of patients that become sick, a certain number will become chronic.

I am all for it; don't misunderstand me, but I am trying to give you the picture. If you skim off those who can be treated and cured rather rapidly, more and more you are building up in the public mental hospitals a backlog of chronic cases.

This is a problem that we are going to have to face. It is not dissimilar from the kinds of complaints you get about some of the geriatric institutions. If this occurs our mental institutions as we now know them are likely to be another kind of hospital. What can you do to move these patients and how do you make this kind of work so attractive that staff will want to work there?

So, over a period of years, a decade or two decades, you could build up in your hospitals as many patients as you have now, made up of just this hard core of chronic patients who have been impervious to treatment.

RESEARCH PROJECT TITLES

Mr. Denton. Just one other thing, and Mr. Fogarty spoke about it. When we have to defend the bill on the floor, some people like to pick out certain names or certain projects and make fun of them. I think about 10 years ago somebody picked out a number of research grants of the Mental Institute, and one of them was about the family life of goats.

Somebody wrote an article about that and it was syndicated all over the country. I remember we had a hearing and it was explained very satisfactorily. I know the man who wrote that article called me up and said he was very, very sorry that he had written that article because he didn't understand the situation.

If these projects were under names that were a little better understood, we wouldn't have that problem.

Dr. Felix. That's right. You have mentioned that project, and just because it is on the record I would like to tell you just a word about it to clear the record.

That project was a study on the difference between young and old sheep and goats in withstanding various kinds of psychological stress. They found out that old goats—speaking of animals—don't stand stress as well as kids—young goats. They also were able to develop a series of prodromal symptoms that the animals showed before they broke down.

The man who did that—Dr. Lidell at Cornell—was called in by the Army to go to Korea and see whether these same symptoms could be found in soldiers who had been in the lines too long and under stress too long.

He found—and this was written up both in the public press as well as the scientific press—that comparable symptoms were found in human beings and you could predict that a person was going to crack if you didn't give him a period of relief from this stressful situation. This was a very worthwhile piece of work.

Mr. Denton. I remember in that case you and the other psychiatrists who appeared made an excellent explanation of the projects. The trouble is that we don't always have those people handy when the question comes up. If they had better names it would help us.

Dr. Felix. Now we do look at the titles, Mr. Denton, to see that they are descriptive and not misleading.

NUMBER OF MENTAL HOSPITALS

Mr. Fogarty. Mr. Michel.

Mr. Michel. Doctor, how many mental hospitals are there in the country?

Dr. Felix. Public mental hospitals, about 280-some. I would like to supply the exact figure for the record.

Mr. Michel. Would you give the figure 10 years ago and what it is today?

Dr. Felix. Yes, sir.

Mr. Michel. Would you also give us your judgment of how many would be needed 10 years from now?

Dr. Felix. Yes, sir. I would like to say here, in giving this, that there is a new concept coming in which may radically change this figure. I support this concept. I am on record in a number of speeches on this.

I believe the most effective hospitals are smaller hospitals, and not these 5,000- or 10,000-bed hospitals. In those the person becomes depersonalized. He loses his identity.

Mr. Michel. What you are doing is recommending against the 5,000- or 10,000-bed hospitals?

Dr. Felix. That's right. I am recommending smaller hospitals, however you have to get them, whether this means programs which will discharge patients more rapidly or breaking up a hospital into two or three smaller ones.

I think any hospital over 3,000 beds is just wrong; and any hospital over 1,000 beds is undesirable; and a 500-bed hospital is much better. I am on record in a number of places—not only myself but others—on that.

So if I could have my way, you would find more hospitals; but they will be smaller hospitals. But I will be glad to supply this.

(The information requested follows:)

Number of Public Mental Hospitals in the United States in 1950 and 1960 and Estimate of the Number in 1970

In 1950 there were 258 public mental hospitals in the United States. This number increased to 280 in 1960. Estimation of the number of public mental hospital beds and the associated number of mental hospitals needed in 1970 is difficult to make because of the fact that we are at a point in time when far-reaching changes are being recommended for the programing of services for the care, treatment, and rehabilitation of the mentally ill. These recommendations relate to the optimum size of State mental hospitals in new hospital construction, revision of the use to be made of existing facilities, and the need for a network of intensive treatment services in general hospitals and other inpatient and outpatient services designed to maintain the patient in the community.

Estimation of the number of mental hospital beds in 1970 requires certain assumptions related to the size of the population of the United States in 1970 and the trend in age-specific resident patient rates between now and 1970. This trend can be affected markedly by care and treatment programs that will be developed in the various States and their subdivisions and the effect these programs (such as psychiatric services in general hospitals, day care hospitals, and other community oriented facilities) will have on preventing admission of patients to or facilitating their release from State mental hospitals. Still another factor is how strong an influence several recommendations made in the final report of the Joint Commission on Mental Illness and Health will have on State programing for the construction of mental hospitals, namely, (1) that all new State hospital construction be devoted to intensive treatment centers of 1,000 beds or less, and (2) that the State mental hospitals of more than 1,000 beds be "converted into centers for the long-term and combined care of chronic diseases, including mental illness."

Utilizing some very conservative assumptions regarding the trend of age-specific resident patient rates, we estimate that in 1970 there will be 528,700 patients in public mental hospitals. This represents a rate of 320.3 per 100,000 population 10 years of age and over in 1970. While this would be a 17-percent decrease from the rate of 385.4 in 1960, the expected increase in the general population will be sufficiently large that by 1970 we would expect a drop of only 6,500 patients from the 535,200 patients in the public mental hospitals at the end of 1960.

If the recommendations of the Joint Commission on Mental Illness and Health were adopted by each State, the acutely ill patients now in the mental hospitals would be moved into smaller intensive treatment facilities and the chronically ill patients would remain in the existing pospitals. In addition, the existing hospitals would begin to admit persons with other types of chronic illness.

A commonly used definition of a chronically ill mental hospital patient is one who has been in the mental hospital for more than 1 year. If we assume that the current proportion of such patients in the mental hospitals will hold in 1970, we would expect 441,400 chronic patients out of the total of 528,700 patients estimated above. Under the recommendations of the Joint Commission on Mental Illness and Health, the existing 280 hospitals would be used for these chronic patients. Provision would have to be made for the gradual replacement of obsolescent physical plants in existing hospitals and the conversion of the present large hospitals into facilities suitable for the care of the chronically ill. The remaining 87,300 patients would be considered acutely mentally ill, and it would require about 90 hospitals of 1,000 beds to provide for their care.

It is emphasized that these estimates are necessarily based on past and current experience and certain operational definitions of acute and chronic mental illness. The actual number of patients in the public mental hospitals in 1970 will depend upon the programs planned and carried out by each individual State and the extent to which the recommendations of the Joint Commission on Mental Illness and Health will be implemented.

NUMBER OF PATIENTS IN HOSPITALS

Mr. MICHEL. What is the number of patients who are in mental hospitals throughout the country today?

Dr. FELIX. The average patient population on any day in 1960 was about 539,000. But we treated, during 1960, 1,350,000 people in hospitals.

ALCOHOLISM

PERCENTAGE OF ALCOHOLIC PATIENTS

Mr. MICHEL. What percentage of those would be attributed to alcoholism?

Dr. FELIX. I will have to supply that. I am not sure. If that had been schizophrenia, I could have told you—about 40 percent. But the alcoholism, I will have to get that. There is a problem with alcohol. You have to differentiate—and sometimes this is hard to do on the reports we get, individuals from admissions—if you get what I mean.

A man may be admitted three times during the year to dry him out. This is one person, one individual, but three admissions. We have difficulty in many cases. They report it by admission, and this is not a true figure of the number of people.

Mr. MICHEL. The reason I ask is that I know at home in one of our State hospitals in Peoria the percentage at one time was quite high. I would like to have it for the whole country.

Dr. FELIX. I remember that.

(The information on the percentage of alcoholics follows:)

Total number of patients and patients with major diagnosis of alcoholism under care in public mental hospitals in the United States during 1959

	Total, all diagnoses	Total, all patients with major diagnosis of alcoholism		Number of patients with diagnosis of—		
		Number	Percent of all diagnoses	Alcohol intoxication, acute brain syndrome	Alcohol intoxication, chronic brain syndrome	Alcohol addiction
Total under care	768,137	56,216	7.3	8,694	18,695	28,827
Resident patients beginning of year	545,150	19,946	3.7	2,409	12,517	5,020
1st admissions	137,976	19,937	14.4	3,691	3,475	12,771
Readmissions	85,011	[1] 16,333	19.2	[1] 2,594	[1] 2,703	[1] 11,036

[1] Estimated for the United States on the basis of data from 21 model reporting area States whose readmissions represent 75 percent of the total readmissions to public mental hospitals in the United States.

PHYSIOLOGICAL STUDIES

Mr. Michel. I was interested in your remarks relative to what studies are being made and contemplated in this area. We know that one who imbibes has slower reflexes and reactions. Have there been any studies to show what brain impairment there is from acute alcoholism?

Dr. Felix. Yes, sir; there have been studies on this. They show that reaction time slows down, and the individual is frequently not aware of this. As a matter of fact, this is one not dissimilar from the barbiturates. He thinks he is functioning better, when, as a matter of fact, he is functioning more poorly.

This discrepancy gets wider the higher the level of blood alcohol, up to a certain point. He thinks he is the life of the party or he is the best man on the golf course. As a matter of fact, he is dubbing half his shots or slicing them into the rough.

Mr. Michel. I want to differentiate between what happens during the time one might be drinking as against permanent damage. Is there real evidence to show——

Dr. Felix. Yes, sir.

Mr. Michel. There is real, permanent damage?

Dr. Felix. This isn't so solid that we can say for sure, but it appears that—there are two kinds of people here, too. You have two kinds of alcoholics. I hate to be so long, but I can't give you a yes or no answer on some of these things.

You have the so-called spree-drinking alcoholic. This is a person who may go for 2 or 3 months perfectly dry and then will go on a binge. He may be on a binge for 2 or 3 days to 10 days or so. Then he sobers up. These people apparently aren't damaged as much as the person who is the so-called steady drinker.

He may consume 2 or 3 fifths a day. I have seen those who consume more. Their nutrition is impaired. They will get to the point where they are drinking and not eating. There may be brain damage; permanent brain damage as a result of this. One will get damage to the peripheral nerves, peripheral neuritis from it. Frequently a psychosis develops.

There is a condition known as Korsakoff syndrome in which the patient becomes quite euphoric. They have peripheral neuritis. They have almost a complete loss of memory for what happened in the immediate past. They substitute for this what we call retrospective falsification. You ask them what they did an hour ago and they give you the biggest story you ever heard about what they did an hour ago, and they weren't even there.

You ask them an hour later what they did 2 hours ago, and they give you a different story.

STATE PROGRAMS

Mr. Michel. Are you satisfied with what the States are doing in this field?

Dr. Felix. The States themselves are not satisfied with what they are doing. They are moving much more rapidly than they were.

This is one of the reasons that we set up the Cooperative Commission on the Study of Alcoholism to study and see what they can do further.

Mr. Michel. In our own State of Illinois we increased the tax on distilled spirits for the express purpose of doing some additional work in this area. Have other States done the same thing? Generally do your studies show where the revenue is derived to carry on this work?

Dr. Felix. I think we can get that.

Mr. Michel. Is there anything that you here at the Federal level recommend to the States in this field?

Dr. Felix. We don't recommend in this area unless we are asked. We recommend a central authority, yes. But as to where they derive their revenue for it, we have never gotten into that.

Mr. Michel. Can you point to anything, any of your activities, which have stimulated the States to take some action?

Dr. Felix. Oh, yes. We have sponsored a number of technical assistance projects in this field. Upon our recommendation, the State has applied for and received a small grant—$2,000 to $4,000—to hold an intensive investigation of their whole situation and a conference on what they can do. We have seen this result in additional clinics, in additional appropriations, and in the setting up of a central authority, and in some modification of the laws relating to this subject. Yes, we have seen that.

Mr. Michel. In response to one of the chairmen's questions you expressed somewhat of a reservation about moving too rapidly in an area for fear that the very support that we gave to a program might give too much encouragement to the layman or cause those across the width and breadth of the land to take too much for granted. Is there a danger of this happening in other fields, do you think?

Dr. Felix. I was speaking about just one area. That was juvenile delinquency. But I was speaking even there about just one aspect of it—that is, wholesale support on a widespread basis of programs which haven't been proved out yet.

In the area of alcoholism, as far as research is concerned, as far as setting up demonstration or pilot clinics or programs, we would be eager to see more of these. We will support these as much as is necessary within our appropriation.

But this is different. This is known to be experimental. But when you say a certain kind of activity is good, this is in effect saying we have investigated this; that it is good; and it can be done safely and profitably.

I want to be sure I don't get in that position unless it is in fact so. If it is so, then I want to do it as hard as I can.

Do I make myself clear? In research, this is a different story. As long as it is an experimental program, fine. But it is when you begin to multiply this and make it widespread as an accepted, valid procedure that I want to be sure before we do it.

DECENTRALIZATION OF MENTAL HOSPITALS

Mr. **Michel.** Getting back again to your recommendation on what size hospitals ought to be, would a consideration in that recommendation of yours be decentralizing the hospitals as much as possible?

Dr. **Felix.** Yes, sir.

Mr. **Michel.** Would there be a consideration of the patient being closer to home?

Dr. **Felix.** That is exactly it. There are two things wrapped up here. In the first, we see more and more—and I think we are more and more successful in getting communities to see—that the responsibility for the mental patient rests in the community.

To whatever degree you remove that responsibility from the community, you are throwing certain barriers in the way of the most complete and thorough recovery.

Now, as you can move hospitals back close to the community, you make it possible for relatives to visit more frequently. Take the hospital in Peoria. It draws from a relatively large area. If that hospital drew from just, say, the city of Peoria and environs and were down to a size of—please; I am in no way criticizing the State or the State's program. I am using this because you happen to know this hospital and so do I. This in no way implies that the State is not doing what it should.

But if that hospital were at a size of 500 to 1,000 and Mrs. Smith's husband is in there, she can take the bus or the streetcar or drive her car and in 15 minutes to an hour be at the hospital. She can see her husband two or three times a week. She can talk to a doctor who knows this case as well as doctors in the community know their patients, because he has a sufficiently small number so that he knows a great deal about each one.

He can work with the family, work with the patient. The patient can go home for a weekend, come back, and go home overnight and come back; go home for 10 days and come back if need be, and move out of the hospital much more quickly.

The doctor in the hospital can be a doctor in the community, too. When you do this, now you have the community responsible for their own and you are bringing the community to the patient, the patient to the community. You are bringing this person back as a productive citizen who can support his family, pay taxes, and who isn't going to be on the other end of it where he is living off of tax money.

INCREASED COSTS OF MENTAL HOSPITALS

Mr. MICHEL. Are mental hospitals as a general rule experiencing the same degree of increased costs in maintenance and operation as the general hospitals?

Dr. FELIX. Yes, sir. As a matter of fact, appropriations are not keeping up with increased costs in most cases. The differential between the per diem authorized in most States and the per diem that is the going rate in general hospitals is very, very wide.

You will find State mental hospitals run from $3 to $4 or $5 per diem per patient, where a general hospital will run $13 to $20 or more.

We don't mean that we are asking all of that for each of these patients, but we do need more if we are going to get a good qualified staff.

Mr. MICHEL. Have any studies indicated what is a proper level?

Dr. FELIX. This is hard to do because what it costs in State A is not necessarily what it costs in State B. For instance, in the American Southwest and in the American Northeast there are some differences in some kinds of costs. This is true elsewhere.

But we can come close to what a level should be for a particular area. But there is no hospital in the country—no public hospital in the country—including St. Elizabeths Hospital in Washington, that is receiving a high enough per capita per diem in terms of the revenue, the funds, that they need to do the kind of job they are capable of doing if they had the funds available.

MENTAL HOSPITAL CONSTRUCTION

Mr. MICHEL. How many new mental hospitals are under construction now throughout the country?

Dr. FELIX. I do not know.

Mr. MICHEL. Could that be answered?

Dr. FELIX. I think I can find out. I know of one in my home State of Colorado that is being built, and they are doing something interesting here. They are building this as a 200-bed unit. They will later add another 200-bed unit, and perhaps a third 200-bed unit. It is to be hoped that it will not exceed that size.

(The information requested follows:)

Complete data regarding the number of mental hospitals currently under construction in the United States is not available. However, through the hospital construction activities, Public Health Service (Hill-Burton program) there are currently three mental hospitals under construction and nine mental hospitals being expanded in the United States.

Mr. FOGARTY. Thank you, Doctor.

INCIDENCE AND COST OF MENTAL ILLNESS

As we have done in the past, we will place your statement on the incidence and cost in the record and, also, your highlights of research during the last year.

(The data referred to follow:)

NATIONAL INSTITUTE OF MENTAL HEALTH

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases dealt with in the National Institute of Mental Health, and the estimated annual cost to the Nation.

I. DEATHS DURING 1959 FOR WHICH SOME FORM OF MENTAL ILLNESS WAS GIVEN AS THE CAUSE (NATIONAL OFFICE OF VITAL STATISTICS)

Category:	*Number*
Psychoses	1,539
Psychoneurotic disorders	90
Personality disorders	2,767
Epilepsy	2,069
Total	6,465

In addition, there were 18,630 suicides. The number of these for which mental disorder was the cause is unknown.

II. DISABILITIES FROM MENTAL ILLNESS

There are not sound nationwide data available on the number of disabilities resulting from mental illness. The following is the number of patients receiving care for mental illness or mental deficiency in the various types of psychiatric facilities at some time during 1959. If it is assumed that each of these individuals was disabled at some time during the year, this would then represent a minimum estimate of disability.

Number of patients receiving care during 1958

Type of facility:	
State and county mental hospitals	767,973
Veterans' Administration hospitals	120,240
Private mental hospitals	84,556
General hospitals with psychiatric facilities	202,252
Public institutions for the mentally deficient	167,616
Private institutions for the mentally deficient	9,829
Outpatient psychiatric clinics	475,000
Total	1,827,466

NOTE.—These data are based on reports received by the National Institute of Mental Health from State agencies, hospitals, and clinics.

III. ESTIMATED ANNUAL COST TO THE NATION

A. Direct cost:	
1. To Federal, State and local governments for care of patients [1]	$1,934,650,000
2. To private agencies and individuals	[2]

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[1] Based on data received from Federal and State agencies responsible for the care of psychiatric patients.

[2] Not available.

HIGHLIGHTS OF PROGRESS IN MENTAL HEALTH RESEARCH, 1960

ITEMS OF INTEREST ON PROGRAM DEVELOPMENTS AND RESEARCH STUDIES CONDUCTED AND SUPPORTED BY THE NATIONAL INSTITUTE OF MENTAL HEALTH

The problem of mental illness has plagued and mystified mankind since earliest times. Yet probably in no area of medicine and science has progress toward basic understanding of causative factors been so arduously slow or painfully achieved. It was more than 2,300 years after the Hippocratic physicians described with remarkable perception some of the classic symptoms of mental syndromes that a comprehensive classification of forms of mental illness was developed. Shackled by superstition, ignorance, and fear, men for centuries despaired of solutions to the enigmas of abnormal behavior. The first great advance in understanding and treatment came in the late 18th century, with the gradual development of the concept of mental illness as a definite sickness based on organic brain pathology. Only as recently as the turn of the 20th century was the role of psychological factors discovered and formulated.

Today, research in the field of mental health and mental illness is extremely diverse. Biological, psychological, and sociological studies are being conducted in a broad multidisciplinary approach to the numerous difficult and unsolved problems. Many of these studies bear an obvious relation to the painstaking task of picking away at the tangled threads of the etiology of mental illness. Other studies are more or less directly aimed at improved methods of treatment and rehabilitation of the mentally ill. But there are many investigations in the field of mental health which, on the surface, have no apparent link to the attack on mental illness. These are the investigations at the more basic level, which attempt eventually to throw new light on the disordered mind. To understand what happens to the disordered mind, it is essential to understand the workings of the human mind under normal conditions, and to understand the human mind, it is essential to understand the many complex interrelationships of the mind with its environment—both the interior physiological environment of the human body and the exterior psychological and sociological environment of the interpersonal world and society. For this reason, much of the research in the field of mental health is basic research, both at the biological and psychological levels, and occasionally several steps removed from the core problems of emotional disorders. These studies seek to find answers from disparate sources which will fit together to make a tool with which to unlock some of the recondite mysteries of mental illness.

This report presents selected findings of research conducted during the past year in the Institute's own laboratories and in many nongovernmental research centers throughout the country which have received support from the Institute.

PROGRESS IN TREATMENT

Mental hospital populations decline

New therapies, including an ever-expanding list of psychopharmacological agents, new techniques both in and out of the mental hospital, and the development of new mental health programs and treatment facilities are gradually reducing the number who must be institutionalized in public mental hospitals.

For the past 5 years, resident mental hospital populations have continued to decline. Data from the Institute's Biometrics Branch indicate that the 535,332 patients resident in the 281 public mental hospitals at end of fiscal year 1960 represented a decrease of 7,389 from the corresponding number at end of fiscal year 1959. This decrease of 1.4 percent compares with a decrease of 0.4 percent between 1958 and 1959, 0.7 percent between 1957 and 1958, 0.5 percent between 1956 and 1957, and 1.3 percent between 1955 and 1956. These figures incorporate the effects not only of the number of releases but also of the number dying and the total admissions occurring within the year. Data indicate that total admissions increased 4.3 percent, 4.8 percent, 7.7 percent, 6.5 percent, and 5.3 percent in 1956, 1957, 1958, 1959, and 1960, respectively, over the previous year; the corresponding percent increases in the number of net releases was 14.6 percent, 3.8 percent, 7.7 percent, 8.5 percent, and 9.6 percent; and the corresponding changes in the number of deaths was 8.7 percent, —2.9 percent, 9.5 percent, —3.3 percent, and 0.3 percent.

Improving the hospital environment

Much attention is being given to the problem of how to make the mental hospital environment more therapeutic. Inservice training programs are improving staff skills and are bringing the benefits of new experiments in hospital administration to more and more mental patients.

For example, an exchange training program among 13 Southern States during the past 2 years has enabled personnel in mental hospitals to observe at first hand new techniques of hospital administration and patient care. The program, conducted by the mental health unit of the Board of Control for Southern Regional Education, was made possible by an Institute grant. Under the program, psychiatrists, psychologists, social workers, nurses, physicians, and other hospital and training school personnel have been given up to 4 weeks inservice training at other institutions.

Laws on mental illness

Much of the current legislation governing commitment and discharge of mental patients interferes with prompt and effective treatment and with their speedy rehabilitation and reintegration into community life. Measures depriving the mentally ill of their civil and other rights represented a confusing patchwork of laws which are a heritage from the past. If modern methods of therapy and rehabilitation are to be effective, the legal hobbles which tend to make invalids of the mentally disabled and prevent their rehabilitation, must be removed.

A major step toward the revamping of legislation dealing with the mentally ill has been taken by the American Bar Foundation, which has just completed a 3-year survey, a major portion of which is a study of all major civil and criminal laws and commitment procedures related to mental illness. The report of this study, to be published under the title of "The Mentally Disabled and the Law," compares statutes, regulations, and court cases dealing with commitment and discharge of mental patients in the various States. Other aspects discussed include determination of the need for protective procedures at discharge, and protection of personal and property rights of committed mentally ill persons under present laws. Legislation pertaining to marriage, divorce, eugenic sterilization, incompetency, guardianship, restoration, sexual psychopathy, and mental disability as related to criminal law also receives attention. A study of voluntary commitments is included.

Building on the groundwork provided by this comprehensive survey, the American Bar Foundation is now conducting a followup study, with the aid of an institute grant, designed to develop model legislation governing care and hospitalization of the mentally ill. Evaluation of existing practices will prepare the way for draft legislation, which can be adopted by the individual States to insure proper treatment of the mentally ill, while at the same time affording adequate protection of their civil rights.

Police training in handling the mentally ill

Because the police often are called upon to deal with the mentally ill, particularly in emergency situations where the ill person may be highly excited and may require immediate hospitalization, a number of communities have instituted special training sessions for the police on this subject. A manual for police officers on "How to Recognize and Handle Abnormal People," prepared a few years ago by Dr. Loyd W. Rowland of the Louisiana Association for Mental Health and Dr. Robert A. Matthews, has been used very successfully in such training programs.

During the past year, with support from the institute, Dr. Rowland and the Louisiana Association, in cooperation with the New Orleans Police Department, produced a new training film for the police entitled "Booked for Safekeeping." This 33-minute 16-millimeter sound film provides basic information needed by any type of law enforcement officer in handling disturbed mental cases, and will assist him in understanding patterns of abnormal behavior. The film depicts average and typical conditions under which the police normally must operate. It contains information useful also to employees of penal institutions and courts. Provisions have been made for widespread utilization of the film by local police departments, law enforcement agencies and associations, and training centers for police officers throughout the country.

Posthospital experience of mental patients

With increasing numbers of patients achieving remission and returning to the community, considerable research activities are directed at developing techniques not only for preventing relapses but also toward improving the level of the ex-patient's personal functioning and adjustment. An intensive study of posthospital experience has been conducted, with Institute support, over a period of years at the Harvard School of Public Health, in an effort to determine what actually happens to patients when they leave the mental hospital. Findings from this study, compiled and published this year by the Hogg Foundation for Mental Health, underscore the importance of evaluating the community milieu.

The role the former patient may be expected to assume in the home, for example, is a critical determining factor. The prognosis for returning husbands is not so good as that for sons. Hospitals releasing incompletely recovered patients to wives are likely to have to readmit them, and alternative community settings for such men are in many instances indicated. The study suggests that a higher proportion of sons now hospitalized might be returned to their families.

Conclusions of the study also suggest a need for appraisal of the practice of releasing patients who are less than well on the assumption that treatment will continue after hospitalization. Investigators found that many patients returned to the community remain there, "preserved like flies in amber," living as it were in one-person chronic wards where they are given custodial care by family members. In such situations these patients are insulated from treatment agencies and other community services. It was found that often the family setting in which the returned patient was tolerated was not therapeutic and rehabilitative, although permissiveness and acceptance were provided. Low-level performance and bizarre behavior on the part of the former mental patient were found to occur most often in those families with low expectations regarding posthospital behavior. A family with high expectations at the time the patient returned, which remained high, was most conducive to motivating the patient to produce a higher level of performance.

The results of the study underscore the urgent need for further mobilization of the interest and efforts of both hospital and community to ameliorate problems in this area. (NIMH grantee, Dr. Ozzie G. Simmons, Harvard University, Reported at meeting of the Texas Association for Mental Health.)

Drug therapy for released patients

Followup studies of released mental patients, conducted under grants awarded by the Institute, have shown that psychoactive drugs, which have proved so effective in hospital treatment of mental illness, can be used successfully in preventing the rehospitalization of chronic schizophrenic patients and in making it possible for them to live at home and hold regular employment. The prolonged treatment procedure is safe, given adequate safeguards, chief among which is proper skilled medical supervision. The drugs used do not appear to bring about adverse side effects nor to impede the patient at his work or learning.

One pilot study was conducted last year by the Research Unit of the Manhattan Aftercare Clinic in New York. A special day hospital facility was set up for the treatment of patients who after release suffered a recurrence of psychotic symptoms. During the year, 26 patients who suffered such relapses were given intensive drug therapy at the day hospital under the supervision of psychiatrists, social workers, and nurses. The required drug dosage was adjusted daily. The patients were given occupational therapy. When family problems were involved, the social worker counseled and helped. In all cases, the psychotic symptoms were brought under control within 6 weeks or less, and the patients were able to return to their duties. Absence for such a limited period did not result in job loss. (NIMH grantee, Dr. Elsa Kris, Manhattan Aftercare Clinic, New York City. Reported at Conference on Drugs and Community Care, Washington, D.C.)

In a 4-year followup study of 330 patients treated with drugs after discharge from the Delaware State Hospital, it was found that only 13.8 percent of those receiving the drug suffered relapses which required rehospitalization, while 47.2 percent of those not kept on treatment had to return to the hospital. (NIMH grantees, Fritz A. Freyhan, M.D., and Joan Merkel, R.N., Delaware State Hospital. Reported at Conference on Patterns of Transition from Hospital to Community, Boston.)

Since psychological and social factors enter into the shifting mental status of a patient under drug treatment, several studies have been designed to separate out the effect brought about solely by medication. Such a study was conducted at the psychopharmocological research unit of the State University of New York. Medication was given, along with biref psychiatric interviews, to 173 schizophrenic outpatients in the form of capsules containing either placebo, promazine hydrochloride, or chlorpromazine hydrochloride. During the course of treatment, 29 patients (16.8 percent) were hospitalized for mental illness. An analysis of the research record showed that 28.6 percent of the placebo patients were hospitalized while 18.2 percent and 4.8 percent of the promazine and chlorpromazine groups, respectively, were hospitalized. (NIMH grantee, Dr. David Englehart, Kings County Hospital, Brooklyn, N.Y. Reported at Conference on Patterns of Transition from Hospital to Community, Boston.)

AVOIDING HOSPITALIZATION

New methods are being tried out in an attempt to obviate the necessity of hospitalizing mentally ill persons when they can be treated on an outpatient basis.

In one community where it has been tried as an experiment, emergency psychiatric treatment in the home, for patients for whom admisison to the State hospital had been requested, has proven to be an effective alternative to hospitalization. When the emergency arises, a team composed of psychiatrist, social worker, and nurse visits the family and works with it as a group and as individuals. Diagnosis and treatment are given by the clinical team when it is felt the patient can remain outside the hospital. During the first 2 years of its operation, the psychiatric home team saw 75 cases for a total of 800 home visits. Eight families were accepted for long-term treatment. The remaining cases were given psychiatric evaluation, brief therapy, and/or referral to other agencies or private physicians. The project was conducted under the direction of Dr. Walter E. Barton of the Boston State Hospital with the aid of an Institute grant.

Another experimental program conducted by the Department of Psychiatry, University of Texas, has shown the effectiveness of brief intensive multiple-impact psychotherapy in permitting outpatient treatment of severly disturbed adolescents. The adolescents who ordinarily would have required long-term psychotherapy or institutional care, have been treated in concentrated 2-day therapy sessions at 6- to 8-week intervals for a period of 2 years. Under the program, the adolescent and his entire family come to the clinic for the 2-day period. Of the 50 adolescents and families followed in the program for a 2-year period, all but 7 showed definite improvements, and 38 adolescents were still living with their families who had effectively mobilized their forces to cope with the youngsters' problems. (NIMH grantee Dr. Harold A. Goolishian, University of Texas Medical Branch. Reported in Social Work.)

Outpatient mental health clinics for years have helped large numbers of people with a wide range of emotional disorders. This year, a report of a survey of ambulatory patients in mental health clinics, the first of its kind so far conducted, reveals that an estimated 379,000 individuals in the United States, including 197,000 children and 182,000 adults, were clinic patients during 1955. One-third of the child patients with diagnosed disorders had transient situational personality disorders. Personality disorders and mental deficiency were frequently diagnosed. Adult patients were usually reported as having a personality or psychoneurotic disorder, although psychotic disorders were not infrequent. Relatively short-term service was provided for many patients. Median number of interviews for children was four; for adults, three. (Anita K. Bahn and Vivian B. Norman, NIMH. Reported in Public Health Reports.)

BIOLOGICAL STUDIES

Biological research in the field of mental illness covers a wide range of studies, including investigations of possible biochemical and metabolic defects, of neurophysiological irregularities, and of basic neuroanatomical structures. Many cogent arguments point to the highly differentiated metabolism of the brain as likely to harbor important chemical mediators of normal and abnormal behavior. Recent years have witnessed the dramatic discovery of a number of neurochemical substances, the biogenic amines, which appear to play an important part in brain activity and the transmission of nerve impulses. Among them are tryptamine, esrotonin, epinephrine (adrenalin), norepinephrine, histamine, and gamma amino-butyric acid. In the process of brain and body function, these biogenic amines are acted upon by enzyme systems which synthesize and destroy them. Much has been learned about the pathways through which these metabolic processes take place. As knowledge of their synthesis, degradation, and distribution is gained, it lays the foundation for comparative studies that may reveal abnormalities that provide clues to mental illness.

Epinephrine and schizophrenia

A major theory formulated in recent years to account for schizophrenia in biological terms has been based on a postulated disorder in the metabolism of circulating epinephrine, with the production of certain abnormal derivatives. This theory was developed at a time when it was possible to account for only a small percentage of the epinephrine released in the body, and only that which was excreted unchanged in the urine. There was no means of measuring the epinephrine altered by body metabolism. To test the hypothesis that a defect in the metabolism of epinephrine might account for the major symptoms of schizophrenia, it was necessary first to ascertain the normal metabolic pathway. In a series of studies continuing over the past several years, investigtaors at the Institute's Laboratory of Clinical Science previously had succeeded in determining the fate of practically all epinephrine administered and also that presumably produced in the body in the form of two major metabolites, metanephrine and 3-methoxy-4-hydroxymandelic acid, accounting for approximately 80 percent, and four minor metabolites including unchanged epinephrine, bringing the total which can now be accounted for to 98 percent in animals and normal man. (Dr. Julius Axelrod, NIMH. Reported in Physiological Review.)

Based on this research, a definitive study of the metabolism of circulating epinephrine in a group of schizophrenic patients was completed this past year. The metabolites in this population were found to be qualitatively identical with that in the normal population, with no evidence for the presence of abnormal metabolites. Only one compound, 3-methoxy-4-hydroxyphenylglycol, was excreted to an extent significantly different from that in normal volunteers (8.9 percent as opposed to 7.1 percent). Conclusions argue against the likelihood that a defect in metabolism of circulating epinephrine accompanies schizophrenia. (Drs. Elwood H. LaBrosse, Jay D. Mann, and Seymour S. Kety, NIMH. Reported in the Journal of Psychiatric Research.)

Metabolism and inactivation of catecholamines

Institute investigators have delineated the metabolic features of the metabolism of the norepinephrine and have elucidated a number of areas in which this metabolism differs quantitatively from that of epinephrine. Even more significant have been findings on the mechanisms of the binding and inactivation of norepinephrine at or near its site of action. In animal studies using injections of tritium-labeled norepinephrine of high specific activity, the researchers have demonstrated a rapid uptake of this hormone by certain tissues of the body which are richly innervated by the sympathetic nervous system. Denervation of such structures results in a loss in the ability to bind norepinephrine, and a number of drugs including reserpine, chlorpromazine, amphetamine, and cocaine have the ability to prevent this binding or to cause the release of bound norepinephrine from these sites. The tranquilizers, reserpine and chlorpromazine, although similar in clinical effects, have very few chemical effects in common. The similar action observed in connection with norepinephrine may provide insights into the mechanism of their psychoactive action. (Dr. Julius Axelrod, NIMH. Reported to the Ciba Symposium on Adrenergic Mechanisms, London. Dr. L. G. Whitby, Rockefeller Traveling Fellow: Dr. G. Hertting, visiting scientist, and Dr. Julius Axelrod, NIMH. Reported in Nature.)

Other clues to schizophrenia

A significant positive finding suggests the presense in plasma of schizophrenic patients of a factor that alters the carbonhydrate metabolism of red cells. During the past year, Institute facilities were made available to a research scientist to apply this test to schizophrenic patients and normal volunteers on the wards. Appropriate analyses were carried out in the Institute's Laboratory of Clinical Science. On the basis of blood samples submitted from 12 schizophrenic patients and eight normal volunteers, and carefully coded to prevent their identity from being known, it was possible on the basis of his findings to predict accurately in a highly significant number the presence or absence of schizophrenia. (NIMH grantees Drs. Charles Frohman and Jacques Gottlieb, Lafayette Clinic and Wayne State University College of Medicine, Detroit. Reported in the American Journal of Psychiatry.)

Role of the biogenic amines

The biogenic amines, which have noticeable pharmacological effects elsewhere in the body, are now known to be differentially localized in various parts of the brain. Although studies in the blood or urine may serve to detect general abnormalities in the metabolism of these agents, if they occur, they are not yet sufficiently sensitive to elucidate their specialized metabolism in the brain. An important new technique has now been developed by an Institute investigator for more precise measurements of metabolic processes. The technique, based on double labeling, employs the use of two different isotopes (radioactive hydrogen and carbon) and may be adopted to yield information on the brain metabolism of biogenic amines from studies of blood or urine. (Dr. I. J. Kopin, NIMH. Reported in Science.)

Another approach employs the administration of certain known precursors of certain biogenic amines in substantial amounts in the diet or bloodstream, in conjunction with drugs which inhibit monoamine oxidase. This would be expected to retard the destruction of the amines and increase their concentration in the brain. Careful behavioral and psychiatric observations of patients under such conditions may serve to elicit mental or behavioral changes which may be characteristic of alterations in specific amine levels. During the past year, such tests have been made on a number of amino acids including tryptophan, phenylalanine, histadine, glutamine, tyrosine, glycine, and methionine, and two more immediate precursors of norepinephrine and serotonin. When approximately 10 times the normal dietary content of these amino acids was administered in successive studies, each for a period of 1 week, two of them were associated with significant behavioral changes in a segment of the patients. Methionine was associated with increased activity and alertness, and an accentuation of some specific schizophrenic symptoms, which was followed by what appeared to be a moderate quiescence of certain symptoms in a number of the patients. Tryptophan, especially in conjunction with the monoamine oxidase inhibitors, produced a relaxation of inhibition and a freeing of association where these had been abnormally marked in several patients. These findings are being further evaluated in order to elucidate their significance to the nature of schizophrenia and the relationship of the biogenic amines to behavior. (Drs. William Pollin, Philippe V. Cardon, and Seymour S. Kety, NIMH. Science, in press.)

Effects of reserpine in nerve cells

Institute investigators, studying the distribution of epinephrine and norepinephrine in the brain nerve cell, have found that they can be separated into two broad fractions: the first present in the cell sap, the second concentrated in granular matter. According to current concepts, the fraction in the cell sap is biologically active; the other is thought to serve as a reserve supply. The effects of the tranquilizer, reserpine, and a number of other drugs have been examined alone, and in combination with each other.

Findings suggest a reappraisal of previous theories on the mode of action of reserpine. The results further substantiate other recent research by Institute investigators indicating that the enzyme, catechol-O-methyl-transferase, takes part in the metabolism of norepinephrine in the brain. (Dr. H. Weil-Malherbe, visiting scientist. Reported in the Journal of Neurochemistry and the Journal of Pharmacology and Experimental Therapeutics.)

Measuring VMA excretion

One of the impotrant accompaniments of human stress is the release from the adrenal gland and the sympathetic nervous system of the important hormones epinephrine and norepinephrine (also known as the catecholamines). A precise method for measuring the amount of these agents released, and correlation with measurements of stress in health and disease, has long been sought. Techniques available for deriving such information have depended on analysis of the hormones per se in the urine. These have been unsatisfactory, since only a small percentage of the epinephrine and norepinephrine released is excreted unchanged. However, the recent identification by Instite investigators of the metabolic products of these hormones has made it possible to estimate more closely, from the residue appearing in urine, the total amount secreted. A new technique has now been developed for the determination of 3-methoxy-4-hydroxymandelic acid (VMA) in the urine of man. Since this compound in urine accounts for approximately 40 percent of injected and presumably endogenously produced epinephrine, it is a much closer indicator of catecholamine secretion in various states. The method has been applied in a number of clinical cases and it has been found, for example, that there is a high excretion rate in patients with involutional depression. A marked increase has also been observed to result from certain drugs or procedures such as reserpine and electroshock therapy. (Mrs. Virginia Weise, Dr. Roger McDonald, and Dr. Elwood H. LaBrosse, NIMH. Clinica Chimca Acta, in press.)

Precise assessments of endocrine function

With the development of a comprehensive battery of hormone measurements at the Institute, precise assessments of adrenal-thyroid function can now be made, and minute fluctuations in their levels can be related to fluctuations in human behavior. The techniques enlarge the possibilities for clarifying the relationships between endocrine function and psychologic stress, which has not been fully understood. Findings, for example, suggest a change in the old concept that adrenal hormones are elevated only as an emergency measure. Research indicates that adrenal hormones sensitively reflect hour-to-hour and day-to-day experiences, and are geared to the stresses of ordinary living.

In a series of psychoendocrinological studies conducted during the past year at the Institute with normal volunteers, involving the relations between endocrine function, normal variation in emotional states, and a variety of psychological stresses both induced and occurring spontaneously, it was found that adaptation to a new environment was a potent stimulus for adrenal activity, as manifested in steroid excretion in urine. Repeated studies over several months have shown that individuals are fairly consistent in adrenocortical function. Some regularly respond to the stresses of everyday living with substantial corticosteroid output. Others under the same circumstances show relatively light response. Mildly pleasant absorptions, such as watching a "bland" nature film, lowered hydrocortisone concentrations in the blood; gripping and arousing films maintained relatively high levels.

Investigation of endocrine correlates of severe psychological stress is also underway at the Institute, in an effort to determine whether other hormones are affected under conditions already shown to be associated with elevated blood levels and urinary excretion of hydrocortisone, epinephrine, and norepinephrine. Output is being measured for aldosterone, androgens, and estrogens, via urinary excretion; and, as an index of thyroid function, blood levels of butanol-extractable iodine are being studied. Findings strongly suggest that substantial changes occur in output of these hormones in distressed states. (Dr. David Hamburg, NIMH. Reported to the Association for Research in Nervous and Mental Diseases.)

Synthesis of melatonin

The pineal gland, a small structure directly in the center of the brain, has challenged the imagination of scientists for centuries. To date its function is unknown. Recently scientists elsewhere have isolated an agent, melatonin, which appears to be highly localized in the pineal gland, apparently the only structure in the brain with the ability to synthesize it. Now investigators in the Institute's Laboratory of Clinical Science, in cooperation with scientists in the National Heart Institute, have demonstrated the mechanism of the synthesis of melatonin by enzymes found in the pineal gland. These enzymes affect the acetylation and methoxylation of serotonin with the production of melatonin. After being formed, melatonin is distributed to all tissues including the brain, and its degration is mainly by 6-hydroxylation, with the excretion of the hydroxylated compound in the urine and bile. Although the function of melatonin in the brain is at present unknown, in lower animals it is known to be the most powerful melanocyte-contracting substance (lightening agent) known. The relationship between these cells, which control pigmentation in lower animals, and brain function is obscure. (Dr. Julius Axelrod, NIMH, and Dr. Herbert Weissbach, NHI. Reported in Science.) (Drs. Irvin Kopin and Julius Axelrod, NIMH; Dr. C. M. B. Pare, visiting scientist, NIMH; and Dr. Herbert Weissbach, NHI. Reported in Biochimica Biophysica Acta.)

Animal disease that mimics multiple sclerosis

Experimental allergic encephalomyelitis, a disorder that can be induced in guinea pigs by intracutaneous injection of brain tissue, offers a useful model for the investigation of multiple sclerosis and other demyelinative or degenerative diseases. An Institute investigator has now succeeded in purifying a water-soluble brain protein from which significant immunologic results have been obtained, suggesting the possibility that the disease may be susceptible to pretreatment as well as suppression after the disease has been induced.

Although all routine immunologic tests on the active protein have been negative, carefully controlled skin testing indicates that intracutaneous injections of aqueous solutions of the protein provide means of suppressing the disease. Other inactive proteins isolated from the brain do not afford this protection. The source of the protein has been traced to the wall of the nerve cell (myelin). The findings open interesting horizons with regard to therapy and prevention of related neurological diseases in humans. (Dr. Marian Kies, NIMH, in collaboration with NINDB grantee Dr. Ellsworth C. Alvord, Jr., University of Washington Medical School, Seattle. Reported at meetings of the Federation of American Societies for Experimental Biology and the American Association of Neuropathologists.)

Isolation stress and brain chemistry

The fact that sensory deprivation causes deviant behavior in man and laboratory animals has long been known. Now investigators have learned that isolation, a form of sensory deprivation, not only produces abnormal behavior in mice but also causes noticeable changes in brain chemistry. Studies on isolated mice have disclosed a significant lowering in phospholipid metabolism in the brain. In view of the fact that chlorpromazine, a tranquilizing drug known to have beneficial behavioral effects in cases of mental illness, is known to stimulate phospholipid metabolism, the findings provide further leads for investigation of the yet unknown relationship between phospholipid metabolism and abnormal behavior. (NIMH grantees Drs. Arthur W. Wase and Jens Christensen, Hahnemann Medical College, Philadelphia. Reported in AMA Archives of General Psychiatry.)

Brain damage and animal behavior

The difficulties in behavior suffered by monkeys when the frontal lobes of the brain are damaged have been traditionally regarded as due to loss of memory. Evidence now suggests that the behavior reaction that ensues may be due to abnormally strong tendencies to repeat actions over and over again (perseveration). It has also been possible to distinguish perseveration from loss of inhibition, and to show that animals with orbital frontal lobe lesions perform more poorly on problems involving inhibition, while those with lateral frontal lobe lesions perform more poorly on problems that involve perseveration. The findings may provide better understanding of the function of the frontal lobe in man, in whom perseveration and inhibition loss is frequently evident following frontal lobe injury, whereas no evidence of memory loss has been found. (Dr. S. Brutkowski, visiting scientist, and Drs. M. Mishkin and H. E. Rosvold, NIMH. Reported to the Eighth Congress of the Polish Physiological Association, Poznan, Poland.)

Behavioral effects of hormone implantation in the brain

A number of hormones are known strikingly to affect behavior, though their mode of action on the brain is far from clear. In an attempt to anaylze the effect of sex hormones on cerebral mechanisms, a guest scientist has developed a method by which a small amount of solid hormone (stilbestrol n. di butyrate) can be implanted directly into the brain of cats. It was shown that implantation of hormone into the posterior hypothalamus markedly alters sexual behavior of such animals. The effect on behavior is specific for the hormone and the site of implanation. Similar implants elsewhere in the central nervous system (or blank implants in the hypothalamus) exerted little or no specific behavioral effect. The distribution of the hormone locally in the brain was studied by the use of radioactive (C14-labeled) hormone. These studies suggest that a small and highly localized area of the brain immediately adjacent to the site of the implant is subjected to a prolonged, steep concentration gradient of hormone; and also suggests that some neurones in the hypothalamus are selectively sensitive to the action of estrogenic hormone. (Dr. R. P. Michael, of London, Rockefeller Traveling Fellow and Guest Scientist at NIMH. Reported to the Fourth International Neurochemical Symposium on the Regional Chemistry, Physiology and Pharmacology of the Nervous System. Varenna, Italy.)

New knowledge of neural function

One of the major mysteries in physiology is how the combination of highly excitable neuron systems in the central nervous system are maintained in orderly activity, and why such disordered discharges as occur, for example, in epilepsy are comparatively infrequent. A series of studies has been conducted in an effort to determine how discharges of these excitable systems are controlled, and what happens when control is impaired and parts of the brain convulse. The hippocampus was selected as site of study because of its exceptional susceptibility to conculsive activity, and and the organization of the discrete layer of pyramidal cells which is thin enough to facilitate insertion of microelectrodes for observation.

A difference in electrical potential across the excitable membrane of a nerve cell is a universal characteristic. Decrease of this difference, known as depolarization, leads to discharge or "firing" of the cell. An increase in potential difference is called hyperpolarization, and is generally accompanied by decrease or cessation of firing of the cell. It is believed that certain inhibitory mechanisms keep the nervous system in orderly action.

Investigations have revealed two fundamental classes of mechanisms of convulsive action. In one, the action is precipitated by afferent stimulation via the fornix. In these cases, the discharge is repetitive, with depolarization sustained for some time and becoming cumulative to a point where the cell can no longer fire. The second type of mechanism was discovered by severing afferent nerve trunks and testing the hippocampal cells after sufficient time had elapsed to allow the afferent fibers to degenerate. At this stage, stimulation of the fornix activates only afferent fibers. This activation, in turn, excites recurrent collaterals, while hyperpolarizing the pyramidal cells and inhibiting them. A rebound effect occurs after stimulation has ceased, accompanied by a period of convulsive activity.

This finding supports the theory that in clinical epilepsy, convulsions are not necessarily triggered by an excessive discharge of neurons but, in some situations, may be caused by excessive inhibition or lack of activity in certain parts of the neural system. (Drs. Eric Kandel and Alden Spencer, NIMH. Reported at meeting of the American Association for the Advancement of Science.)

Localization of procreative function in the brain

Although the brain has been extensively explored by electrical stimulation, little has been learned until recently about the neural mechanisms involved in such an important function as sexual arousal. Knowledge of the cerebral localization of this function would be of value in a further search to identify structures involved in related manifestations and in social behavior conducive to the preservation of the species.

Earlier studies identified certain positive loci for such activity along a major pathway of the limbic system passing through the septum, the medial preoptic region, and the lateral hypothalamus. Further observations reported this year indicate that positive loci also exist in parts of the anterior and midline nuclei, along the course of the mammillo-thalamic tract, at points impinging on the mammillary bodies, and in the ventral tegmentum.

The implications of these findings are of considerable interest, as the mammillo-thalamic tract, which is not found in the reptilian brain, is confined to the mammal, and attains its greatest size in man. Heretofore the mammillo-thalamic tract has been looked upon as one of the silent areas of the brain, for which no known function has been established. In addition to the mammillo-thalamic pathway, the medial part of the medial dorsal nucleus has also been shown to be specifically involved in sexual arousal. It has been known that an important neural channel exists between the medial dorsal nucleus and the frontal lobes of the brain, and that the frontal lobes play a role in anxiety and tension states. (Dr. Paul D. Maclean, NIMH. Reported to the Federation of American Societies for Experimental Biology.)

New method for measuring CBF

A new technique, utilizing the radioactive gas krypton, for rapid continuous measurement of the flow of blood through the brain has been devised by a team of scientists at the Aviation Medical Acceleration Laboratory, U.S. Naval Air Development Center, Johnsville, Pa., in collaboration with scientists from NIMH. The method represents a significant advance over the standard nitrous oxide technique in that it makes possible the measurement of total blood flow minute by minute, with detection of abrupt changes in cerebral circulation as they may occur.

In the studies reported, the gas was inhaled by 10 normal young men and measurements of krypton in the brain were taken with a scintillation counter precisely located with respect to the brain and shielded to exclude radiation from other body areas. Results showed close correlation with those obtained by the nitrous oxide technique.

The new method broadens possibilities for more detailed analysis of changes in the rate of blood flow through the brain, with possible implications this may have for both normal and abnormal mental states. (Drs. Benjamin Lewis, Richard Wechsler, and W. Budd Wentz, U.S. Naval Air Development Center, Johnsville, Pa.; and Drs. Louis Sokoloff and Seymour S. Kety, NIMH. Reported in the Journal of Clinical Investigation.)

Direct current changes on cortex

Direct current (d.c.) changes on the surface of the cerebral cortex following sensory stimulation have been variously reported. These changes are quite distinct from the fast electrical changes observed by conventional electroencephalographic techniques. Their interest lies in their possible, though as yet undetermined, relation to sensory function.

Using a compact, sensitive, and stable nonpolarizable calomel electrode of his own design, and special d.c. amplifiers, an Institute investigator has developed a method for recording these phenomena in the lightly anaesthetized and in the conscious animal. He has shown that these d.c. changes are highly sensitive to experimental conditions; but that, with proper care, they can be regularly obtained even in the conscious animal. The characteristics of these changes have been defined. The response to auditory stimulation in various areas of the brain has also been studied. The method represents a definite technical advance in the study of d.c. changes on the surface of the brain and their relation to the processes of attention, sensory discrimination, and the effects of drugs influencing sensory function. (Dr. R. G. Gumnit, NIMH. Reported to the EEG Society and in the Journal of Neurophysiology.)

Physiologic functions of sleep and dreaming

In recent years evidence has accumulated that dreaming is not an occasional and unpredictable occurrence, as has been commonly believed. This assumption gave way before the discovery that dreaming is associated with a specific pattern of brain waves and eye movements which can easily be recorded without disturbance of sleep. The application of this technique disclosed that dreaming is a highly regular and intrinsic part of normal sleep, occurring in scheduled periods over the night, each lasting from 5 to 70 minutes, and taking up an average of 20 percent of sleeping time. That dreaming is necessary to well-being is suggested by the findings that, if a sleeper is prevented from dreaming over a series of nights by being awakened whenever he begins to dream, there is a progressive increase in the number of his dream attempts, and he makes up for the dreaming lost by dreaming more when allowed to sleep without interruption.

These findings have been confirmed at the Institute, and additional studies have been undertaken to further clarify the physiological accompaniments and functions of dreaming. It has been demonstrated that dreaming is associated with striking changes in other physiological indices, such as respiratory rhythm, heart rate, and skin temperature. The extent of this pervasive physiological upheaval seems to be variable and roughly predictable, depending upon the duration of sleep and the degree of fatigue of the dreamer. It may relate to whether, or how clearly, dreams are remembered on awakening. Continuing studies will attempt to answer such questions as how the dream experience is related to the depth of sleep, and whether derangements in the sleep and dreaming patterns might contribute to the precipitation of mental illness. (Drs. Frederick Snyder and David Hamburg, NIMH. Reported to the American Psychiatric Association.)

PSYCHOPHARMACOLOGY

The psychoactive drugs discovered in recent years, which affect mental states and behavior, have provided the scientist with a dramatic new tool not only for clinical application in therapy but for the elucidation of brain function. Such drugs include the tranquilizing and energizing drugs which are utilized in the management and control of mental disorders. An understanding of their mode of action, as yet not fully understood, may throw light on the processes that mediate behavior. Another class of drugs, the psychotomimetic agents, produce transient psychoticlike states. Under their influence, normal people experience such typical manifestations of mental illness as hallucinations, delusions, and feelings of unreality and dissociation. Solution to the question of how these psychotomimetic compounds work on the metabolism of the brain and nervous system should provide significant clues to what happens in true psychotic states. An extensive research program in psychoactive drugs is underway at the Institute, and, with its support, at other research centers. The research involves both clinical evaluation of such drugs and studies of their basic mechanisms of action.

Psychopharmacology Service Center

The Institute's Psychopharmacology Service Center stimulates and coordinates clinical and basic research on psychoactive drugs. It is expanding support for early clinical drug-screening activities, and increasing the number and capacity of clinical facilities available for testing such compounds after adequate animal screening by the pharmaceutical industry. An active program also has been undertaken to provide scientific information to investigators conducting psychopharmacological research.

A cooperative drug study was launched toward the end of the year in nine hospitals. Data will be compiled on a comparative effectiveness of three "tranquilizing" drugs—chlorpromazine, fluphenazine, and thioridazine. Investigators report that fluphenazine, a high potency phenothiazine derivative which is 100 times as potent as chlorpromazine, produces a high incidence of neurological side effects. Thioridazine, equal in potency to chlorpromazine, seems to produce almost no side effects. Fluphenazine was developed by both the Squibb and the Schering Pharmaceutical Cos., thioridazine by the Sandoz Pharmaceutical Co. The cooperative drug study, utilizing a wide variety of clinical settings, is expected to provide results of broader value than could be achieved by a single study in any one hospital. A data-processing unit has been established at George Washington University to analyze material from this and other research projects.

Phenothiazine dosage study

A new contract between the Psychopharmacology Service Center and Temple University, Philadelphia, is expected to help investigators determine optimum dosage for chlorpromazine, one of the most commonly used phenothiazines. The University's Research Institute will synthesize metabolic products of this potent tranquilizer in order to provide tools for a better understanding of the relationship between its metabolism in the body and its therapeutic action. These metabolic products have been tentatively identified in microscopic quantities in the urine of patients and animals treated with chlorpromazine, but larger quantities of known chemical structure are required for precise identification. The synthetic metabolites will be used as standards of comparison at hospitals where the excretion rate and characteristics of phenothiazine metabolites are under study.

New drug assay method

Research into the clinical efficacy of antidepressant drugs will be speeded up by a new chemical assay method developed by scientists at the NIH. An unusual chemical substance, kynuramine, synthesized by a new and rapid route by NIAMD scientists and made available to researchers through a contract negotiated by NIMH's Psychopharmacology Service Center, has been put to use for measuring the activity of the enzyme monoamine oxidase which plays a significant role in body metabolism. This enzyme acts upon pharmacodynamic amines and exercises a regulatory function peripherally as well as within the central nervous system.

Some of the drugs that have proved to be useful in the treatment of depressed patients are also known to have an inhibiting effect on the action of monoamine oxidase. It is not known whether there is a relationship between the inhibiting effect of these drugs on monoamine oxidase and their effectiveness in the treatment of depression. This is an area of research, however, in which there is great interest and vigorous investigation at the present time.

The new technique will greatly facilitate such research efforts. Procedures previously used for measuring monoamine oxidase enzyme activity depended upon difficult and somewhat tedious measurements of either tissue oxygen uptake or substrate amine disappearance. Cumbersome analytical methods are involved in the measurement of amine disappearance. The measurement of oxygen uptake requires manometric assay procedures which also have certain limitations. The new assay using kynuramine utilizes a spectrophotometric method which makes it possible to determine rapidly and accurately the disappearance of kynuramine or the formation of 4-hydroxyquinoline (to which kynuramine is converted as a result of monoamine oxidase activity). The new method can be applied to crude tissue extracts and appears to be a highly suitable tool for the assay of monoamine oxidase activity.

The new method was developed by NIH scientists. It was made possible by a contract-grant from the National Institute of Mental Health through its Psychopharmacology Service Center. Scientists in NHI and NIAMD obtained the first sample of the rare substance, kynuramine, by a novel and rapid synthetic route from tryptamine. Through the contract which the Psychopharmacology Service Center had negotiated with the Regis Chemical Co., it was possible to promptly prepare a substantial amount and samples of kynuramine were made available to the NIH workers. The Regis Co. was also able to make enough of the compound to offer it for sale to other research investigators. (Drs. Herbert Weissbach, Thomas E. Smith, and Sidney Udenfriend, National Heart Institute, and Drs. John W. Daly and Bernhard Witkop, National Institute of Arthritis and Metabolic Diseases. Reported in the Journal of Biological Chemistry.)

New powerful psychotomimetic drug

Psilocybin is a new synthetic pharmacological compound structured after the active ingredients in an intoxicating mushroom long used by the Indians in Mexico. Its ability to produce hallucinations similar to those experienced in schizophrenia makes it a drug of great research interest. Recent studies have explored the range of its effects, with emphasis on dosages up to 36 mg. Healthy volunteers were used to get a clear picture of drug action unobscured by psychotic symptomatology. In these ranges the drug was found to produce perceptual, affective, cognitive, behavioral, and autonomic responses qualitatively similar to those previously described with lysergic acid diethylamide, but a greater degree of impairment of cognition.

Twelve of fourteen subjects reported visual hallucinations, 9 reported visual delusions, 2 auditory delusions, 10 described body image distortions. Emotional reactions ranged from marked euphoria through anxiety and depression. Marked impairment in verbalizing and disorganized thinking was evidenced. The possibility exists, investgiators state, that this may have been related to dosage or personality difficulties.

The studies underscore the potential hazard in use of psychotomimetic drugs as therapeutic agents in outpatient settings. Acute stages of excitement, depression with suicidal ideation, and impairment of judgment may occur with these drugs, even in a carefully supervised setting. The danger of self-administration and inadequate supervision could compound such occurrences. Further research is indicated regarding the site of action of hallucinogens, relationship between personality, dosage level, and total behavioral pattern, and their possible prognostic value in assessing susceptibility to mental illness. (NIMH grantee, Dr. Sidney Malitz, Department of Experimental Psychiatry, New York State Psychiatric Institute. Reported in Comprehensive Psychiatry.)

Method for classifying psychotomimetics

Further evidence that psilocybin induces a temporary psychosis by acting on the same mechanisms within the brain as does lysergic acid diethylamide (LSD–25) has been obtained by investigators at the Institute's addiction research center. The evidence was provided by studies showing that cross-tolerance developed between the drugs. Such studies previously have been used to establish the biologic similarity of synthetic narcotics to morphine.

Patients who received LSD daily for periods of 6 to 12 days showed little reaction to LSD, and at the same time showed a markedly diminished reaction to psilocybin. Conversely, patients made tolerant to psilocybin by treatment for the corresponding period of time showed markedly reduced reactions to LSD. The research suggests that studies of tolerance and cross-tolerance may be useful in classifying psychotomimetic drugs into definite groups. Within a group, the drugs should show a high degree of cross-tolerance, with little cross-tolerance between drugs from different groups. If so, this might lead to correlations between psychotomimetic effect and biochemical or neurophysiological processes in the brain, eventually pointing the way to an explanation of how these drugs create psychic aberrations. (Drs. Harris Isbell, A. B. Wolbach, A. Wikler, and Mr. E. J. Miner, NIMH Addiction Research Center. Reported at regional meeting of American College of Physicians, Lexington, Ky.)

Effects of psychotomimetic tryptamine derivatives

The mode of action of the psychotomimetic drugs which induce transient mental changes in man is of great theoretical and applied interest. The theoretical interest derives from the need to understand the chemical changes a drug undergoes in the body, and the effects of the compound, or its metabolic products, on the brain. The applied interest rests in the hope of antagonizing the effects of a drug through a biochemically related compound. A new type of psychotomimetic compound has been investigated at the Institute by a research worker who first observed the striking transient mental changes induced in man by dimethyl and diethyltryptamine 4 years ago in Hungary. The interest of these compounds lies in their chemical structure, since both are closely related to indole compounds (such as serotonin) known to occur naturally in the animal body and in the brain.

His studies have shown the endogenous conversion of diethyltryptamine into a more active derivative (6-hydroxyldiethyltryptamine). This finding provides one of the very few known instances of the endogenous conversion of a psychotomimetic compound into a more active rather than a less active derivative in the animal body. Furthermore, joint studies with a behavioral scientist have shown that the rate of this conversion differs from animal to animal in the same species, and that this difference in rate corresponds to differences in behavioral threshold for the parent substance. The higher the rate of biotransformation to the 6-hydroxy derivative, the less of the parent substance was required to produce a given behavioral effect in a particular animal. These findings provide a sound experimental setting for combining behavioral techniques with metabolic exploration in the individual animal. (Drs. Stephen Szara and Eliot Hearst, NIMH. Reported at meetings of the Federation of American Societies for Experimental Biology and the American Psychological Association.)

Effect of secobarbital on athletic process

Numerous laboratory investigations have shown that barbiturates and other drugs alter performance on psychomotor and mental tests. Recent studies were designed to determine the effects on judgment of amphetamine and secobarbital. These drugs have long been used as a stimulant and a sedative, respectively. By comparing an athlete's actual performance with his personal judgment of his performance, it was possible to examine a complex process of judgment in a situation in which performance and judgment were matters of personal importance.

Fifteen college swimmers swam 360 time trials receiving 100 mg. of secobarbital, 14 mg. of amphetamine, or a placebo on different occasions. Each was a highly trained athlete in midseason form who was skilled in estimating performance time. After each trial the swimmers estimated their performance time and gave a detailed evaluation of their performance. Secobarbital significantly impaired performance, and amphetamine significantly improved it. The subjective data showed that secobarbital produced distortion in judgment. After taking secobarbital, swimmers thought their performances were unusually good, whereas in fact they were unusually bad. The effect of amphetamine on judgment was not conclusive. The profound impairment in judgment due to secobarbital was produced when the subjects swam in groups of three. Solo swimmers taking amphetamine thought their performance was about the same after amphetamine as after placebo. Actually, amphetamine had significantly improved it. (NIMH grantees Drs. Gene M. Smith and Henry K. Beecher, Harvard Medical School. Reported in the Journal of the American Medical Association.)

Psychomotor effects of meprobamate

Although administration of meprobamate (a mild tranquilizer developed by Wallace Laboratories) has not been found to affect driving ability for normal subjects adversely, a slight but significant decrease in psychomotor activity performance has been found among anxious neurotics. Research has disclosed that with subjects psychiatrically diagnosed as anxious neurotics, chronic dosages of meprobamate led to slowed reaction time in simulated driving at high speed, accompanied by a slight lowering in accuracy. Investigators suggest that increased ability to concentrate, produced by the meprobamate, may have resulted in a concomitant decrease in ability to shift attention. Since these findings differ from those observed with normal subjects, they suggest the possibility that this effect of meprobamate may be specific to anxious neurotic patients. (NIMH grantees Drs. Leonard Uhr, John Pollard, and James Miller, University of Michigan. Reported in Psychopharmacologia.)

Drugs of limited value with disturbed children

Reports from recent studies have raised questions regarding the effectiveness of the use of tranquilizing drugs, successful with adults, in treating children with behavioral problems. Treatment with meprobamate and prochlorperazine have been observed to provide no evidence for the superiority of either drug over placebo. Prochlorperazine was developed by Rhone-Poulenc Laboratories in France, and marketed in the United States by Smith, Kline & French. More recently comparative studies by the same investigators have been conducted to determine the effectiveness of psychotherapy alone and in conjunction with a new agent, perphenazine, or placebo in treating neurotic or hyperkinetic (overactive and distractible) children. Perphenazine was developed by Schering Laboratories.

Whether on perphenazine or placebo, two-thirds of the neurotic group, and one-third of the hyperkinetic group demonstrated significant improvement. The findings suggest that the diagnostic differentiation between neurotic and hyperkinetic is important in predicting outcome of patients receiving brief outpatient treatment.

Investigators noted that the prompt and usually satisfactory response of neurotic children to brief psychotherapy left little room for any but the most remarkable drug to demonstrate its effects. More effective pharmacologic agents are being sought for use with hyperkinetic children who do not respond so well to psychotherapy. (NIMH grantee Dr. Leon Eisenberg, Johns Hopkins University. , Reported at annual meeting of the American Psychiatric Association.)

Clinical studies in a mental hospital setting

Drug studies carried out in the Institute's Clinical Neuropharmacology Research Center at St. Elizabeths Hospital have centered on problems related to the management and treatment of the chronic schizophrenic patient, a dominant problem in a mental hospital.

A comparatively drug study, involving two tranquilizers and a placebo, was initiated simultaneously on six wards of the William A. White Service. The investigation was also planned to examine in detail, and with an emphasis on quantitative assessment, the effects of nondrug factors known to affect profoundly the efficacy of drugs in a typical mental hospital setting. Essentially, the study thus aimed at: (1) Determining the effect of physical environment on responsiveness to drugs; (2) determining the effect of various types of nursing care (and particularly nursing in small groups) on drug response; (3) the cultivation of native therapeutic and research skills often found, but ignored, in ward personnel; (4) the codification of a number of questions commonly entering into a drug trial, including selection of patients, selection of drugs, selection of experimental design, technique of drug administration in a blind study, assessment of side effects, management of adequate laboratory control, and the comparative examination of a number of clinical evaluative techniques; (5) the monitoring of attitudes toward research; and (6) the institution of data reduction and statistical techniques best suited to such a drug study. The dimensions of the study were kept within the limits of applicability and feasibility to a State hospital setting, so as to make possible a retesting of the conclusions throughout other services of St. Elizabeths Hospital and other State hospitals.

A quantitative analysis of data is now proceeding. Several trends, however, are clearly apparent. A coordinated program of clinical investigations proceeding simultaneously in a number of wards of a mental hospital building (rather than a single research service) can profoundly, and with great economy contribute to the raising of both therapeutic and research skills of personnel throughout such a building. Nursing in small groups, structured around the skills of attendants and of cooperative patients, can act as a pacemaker in changing the therapeutic climate of a chronic ward, and usefully contribute to the rehabilitation of patients. Such a regimen also reduces consumption of tranquilizers on a ward. The use of suitably designed documents enhances the observer skills of personnel, while at the same time providing quantitative data which can be subjected to machine analysis.

The wider application of the study was shown by its replication on a more extended scale in 126 very deteriorated patients. Group nursing techniques and drug research designs developed in the Service have also been applied in other parts of St. Elizabeths Hospital. With the cooperation of the Medical Arts Section, National Institutes of Health, an extensive teaching and demonstration exhibit was prepared, based on the initial study, and was exhibited at meetings of the American Psychiatric Association and the American Medical Association. (Drs. A. Hordern and M. Hamilton, visiting scientists, NIMH; Dr. J. Lofft, NIMH; and Dr. F. N. Waldrop, St. Elizabeths Hospital.)

CHILDHOOD STUDIES

Because of the significance of early formative years for later adjustment, much of the behavioral research of the Institute is focused on child development and patterns of family living and social interaction that play a determining role in influencing the direction of growth.

Seeking clues to child behavior

A unique series of studies to determine the predictability of certain child behavior patterns, based on a knowledge of how he reacts at birth and of factors in the parents' marriage relationship, has been underway this year at the Institute's Biosocial Growth Center. The studies are part of a long-term research program which will also concentrate on the child's extrafamilial relationships, and an evaluation of the influence of other events occurring during infancy and early childhood.

The prenatal family environment is being charted with the cooperation of 40 newlywed couples, who have been observed both at home and at the Institute. Techniques that have been developed to provide information include experimental situations, psychodrama, and questionnaires and interviews. As children are born into these families their behavioral patterns will be observed from the earliest manifestations of infant personality, with special regard to feeding habits and skin sensitivity. Earlier studies have indicated that these characteristics may provide significant clues for the prediction of subsequent behavior.

Interrelation of maternal and child behavior

The influence of a mother's behavior on child development has been examined over a period of years and has recently been reported in a study on environmental influence on personality. Findings are based on data collected in California on 54 subjects from birth to adulthood, and analyzed at the Institute.

Studies on the consistency of attitudes over a period of time show that a mother's acceptance or rejection of a child remains relatively the same from infancy through preadolescence. Attitudes of permissiveness or control may vary, however. Child behavior as to extraversion or introversion is rather consistent through childhood; it is not so as regards adjustment or maladjustment.

Findings suggest that parental attitudes of permissiveness or constraint may be less important factors in relation to a child's overall adjustment than has been thought. Much more important appears to be the degree to which a child is accepted or rejected by his mother.

Family socioeconomic status also appears to be less related to the child's behavior than his mother's attitude toward him, though it may play a part, along with financial stress and health, in determining maternal behavior. How a mother reacts to her son during infancy is more closely related to his adjustment at 9 and 12 years of age than is his own infant behavior, suggesting that early maternal patterns may be more predictive of the child's future adjustment than is his own early behavior.

In the families studied, boys appeared to have been more influenced by the way they were handled by their mothers in infancy than were girls. Girls seemed to be more affected by current maternal behavior, suggesting that girls respond more to their current interpersonal situation, while boys tend more to reflect past relationships. (Drs. Nancy Bayley and Earl S. Schaefer, NIMH. Reported at the 1960 Regional Research Conference on Child Development of the American Psychiatric Association, at the University of Iowa.)

Allocation of parental responsibilities

Most theories of personality development have been based on a model of a family in which the role of mother and father are necessarily differentiated, with mother specializing in providing emotional support and father in imposing restraints. Present research, however, on social class and parental responsibility indicates that both middle-and working-class variations on this theme are sufficiently great to compel a more precise formation.

Previous data have disclosed decidedly different emphases in middle- and working-class values for children. According to these findings, the dominant motif of middle-class parents' values is that the child develop his own standards of conduct; of working-class parents, that the child's actions be reputable. Further studies by the same investigators reveal that, in a sizable proportion of middle-class families, it is mother who takes primary responsibility for imposing constraints on sons, and father is at least as supportive as mothers. Fathers are seldom as supportive of daughters as are their wives.

While it would be an exaggeration to state that middle-class fathers have abandoned the prerogatives of authority in favor of being friend and confidant to their sons, this research suggests that the historical drift is probably toward primary emphasis on support. It supports the conclusion that today in middle-class families, mothers' and fathers' roles are not sharply differentiated. To the degree that they are, a new division of responsibilities is developing, with each parent being most supportive of children of his or her own sex.

Mothers' and fathers' roles are more sharply differentiated in working-class families, with the children almost always feeling that mother is the more supportive parent. Yet fathers do not specialize in setting limits, even for sons.

In most working-class families, mother raises the children, father provides the wherewithal. The studies reported indicate that this pattern of role allocation is probably far more prevalent in American society than has been recognized by the formal theories of personality development. (Drs. Melvin L. Kohn and Eleanor E. Carroll, NIMH. Reported in Sociometry.)

Birth order and schizophrenia

Data supporting a relationship between birth order and schizophrenia, which has been hypothesized by other investigators, have been produced in a study of hospitalized schizophrenics conducted by an NIMH investigator. Among a cross section of female schizophrenic patients, it was found that significantly more patients came from the last half of their sibling group than from the first half.

If a relationship between birth order and incidence of schizophrenia does in fact exist, as the studies indicate, the problem of finding the cause yet remains. One possibility which the investigators discuss is that the apparent effect of birth order may be merely an artifact of the relationship between the increasing age of the mother and incidence of schizophrenia. Both physiological and psychological explanations are possible. Explained in terms, it is possible that increasing age and large numbers of children may affect the intrauterine environment in such a way as to leave the child with a physiological predisposition to the disease. Explained in psychological terms, it is possible that younger children coping with anxiety may have less access to their parents. (Dr. Carmi Schooler, NIMH. Archives of General Psychiatry, in press.)

Childhood enuresis

Evidence disputing the traditional view that childhood enuresis is a sympton of emotional instability has been produced by Washington University and the St. Louis County Health Department. In a study of 830 children at the 8- and 9-year age level regarded as bedwetters, assessment made on the basis of information provided by teachers, mental health personnel, and families show very low correlation between this habit and other symptoms of psychological disturbance. In no instance did the study show to any significant degree that enuretics have greater maladjustment than nonenuretics, or that enuresis can be regarded as more closely associated with emotional symptoms than is thumbsucking. The conclusions do not hold for adult enuretics, in whom a correlation with psychopathology has been found. They serve only to show that there is little justification for assuming that bedwetting continued into the ninth year suggests emotional disturbance. (NIMH grantee Dr. F. Tapia, St. Louis County Health Department; J. Jekel, Washington University School of Medicine; and Herbert R. Domke, Allegheny County Health Department, Pittsburgh. Reported in the Journal of Nervous and Mental Disease.)

AGING

With the increasing complexity of society, certain specific problem areas such as aging have emerged that have relevance to mental health and mental illness. With many other groups, the Institute shares a continuing concern for these areas and seeks to initiate and coordinate research programs that will not only provide fuller understanding of the processes involved, but will to some extent help to restore to society some of the human potential now lost.

New psychological theory on aging

Much recent research has focused on the psychosocial aspects of aging, in an effort to gain further insight into the nature and extent of psychological changes that occur in the aging individual. A major study, reported on this year, has been conducted in Kansas City by the Committee on Human Development of the University of Chicago, on a grant from the Institute. Observations have been made over a 5-year period on 211 persons, including a panel of healthy adults between the ages of 50 and 70, and a group of ambulatory old people between the ages of 70 and 90.

From the intensive study of findings there has emerged the theory of "disengagement," in which aging is seen as an inevitable mutual withdrawal or disengagement, resulting in decreased interaction between the aging person and others in the social system to which he belongs. The process may be initiated by the individual or by others around him, and he may withdraw more markedly from some classes of people and remain relatively close to others. His withdrawal may be accompanied from the outset by an increased preoccupation with himself. Certain institutions in society may make this withdrawal easy. But when the aging process is complete, the equilibrium that existed in middle life between the individual and his society has given way to a new equilibrium characterized by a greater distance and an altered type of relationship. The investigators theorize that some intrinsic change may occur with age which is the analog of maturation in children, which brings about this loss of involvement or disengagement from the environment. The disengaged state appears to be an almost universal end point, and it appears to be irreversible.

The theory differs from the traditional theory of aging which assumes that the aged person is isolated through desertion by others in his social structure, and that the constricted world of the aged is not of his own choosing. The disengagement theory suggests that he is not merely subjected to a shrinking universe, but participates in creating it. The hypothesis of disengagement indicates a reappraisal of some of the common assumptions associated with the "activity" theory of aging. For example, a widely held concept that successful aging consists in continuing middle-aged activities as much as possible may not be valid. Many old persons, the study showed, do not desire an extension of continued usefulness, or the development of new interests and new contacts. They find equal satisfactions in their more confined spheres of activity.

In the process of disengagement, specific changes were observed to take place, contributing to the aged person's becoming less bound to the social system of which he is a member. A shift in perception occurs in the sixth decade which may reflect both a withdrawal of intense emotional attachment to objects and people, and a beginning of anticipation of the aged state. This shift is accompanied by a constriction is the variety of social interactions undertaken, and is followed shortly after by a reduction in the number of hours spent in the company of others.

Concomitantly, relationships gradually become redefined so as to be less like those of family, work, and voluntary associations and more like those of recreation. A change in behavioral motivation becomes apparent. Desire for approval and love, the typical rewards of work and kinship, strikingly lessen with old age, and a new freedom of choice of rewards emerges, with a tendency to select short-run gratification such as are found, for example, in recreational activities. The theory, postulating a lessened concern for social approbation and desire for esteem in advancing years, helps explain the self-centered and idosyncratic styles of behavior often noted among the ambulatory aged (NIMH grantee William E. Henry, University of Chicago; reported in Sociometry by Dr. Elaine Cumming, project coordinator).

Research seminar on aging

In the summer of 1960, an International Research Seminar on the Social and Psychological Aspects of Aging was held in Berkeley, Calif., in conjunction with the Fifth International Gerontological Congress. Institute support was provided for travel grants for foreign participants and for publication of the proceedings, and the program was jointly developed by the Professional Services Branch of the Institute and the division of gerontology of the University of Michigan.

Research presented and discussed at the seminar included recent studies on the psychological capacities of the aged, including perceptual and thought processes; personality, life styles, and social roles, focusing on how older people participate in social processes and how this changes with age; mental health and rehabilitation; and health aspects of income, employment, and retirement.

Adaptive capacities of aged

Changed capacities and changed circumstances that characterize old age impose limitations and require reorganizations and substitutions in behavior. The predictable structure of everyday living in terms of the routine responsibilities and motivations relating to family, work, and community breaks down, and a new structure must be built to replace it. A physical organism, itself undergoing change, must deal with often major changes in its social environment.

This study focused on the adaptive capacities of a group of healthy aged men to their changed social environment. The relative good health possessed by all in the sample population was not correlated with a homogeneity of well-being in personal social functioning. Both hopeless resignation and creative involvement were found among persons studied. Some had withdrawn to routines and self-centeredness, others were engaged in varied and absorbing activities.

Previous educational and occupational levels and ethnic classifications did not appear to affect the capacity of an aged person for social functioning. Though at the height of their careers the ways of life of a professional person and an unskilled worker had differed markedly, by the age of 70 the elements of day-to-day activities and attitudes about being old had merged into similar general patterns. This "leveling" results partly from the tendency for these men to drop their specializations, find similar hobbies, use common recreations afforded by culture, and engage in many "maintenance" activities of the household. Inner resourcefulness was by no means solely the property of the more educated.

In only one respect did educational factors appear to relate clearly to present adaptation: There was a significant association between education and relationships with children. Conflict and feelings of rejection were found more frequently between the less-educated men and their children. Studies of individual cases suggest that discrepancies in educational and cultural level of parent and grown children, rather than low education per se, characterize the families for whom conflict is accentuated. Extensive cultural displacement from conditions of early childhood also tends to handicap certain adjustments.

Success in working careers interpreted as evidence of adaptability and striving appeared to be predictive of greater adaptability to the stresses of aging. Men who advanced in their jobs showed different adaptations from those who did not move upward—having more complex and varied living patterns and enjoying better relationships with their children in old age.

In studying the processes by which the subjects had retired from active work, it was evident that fewest difficulties resulted when the decision to retire had been made voluntarily by the man himself, or was controlled institutionally. Those who arrived at retirement through conflicting pressures suffered most ill effects.

Immediate environmental factors were, as expected, found to be closely related to the aged persons' behavior and attitudes. Loss of loved ones, loss of income, and cultural displacement considerably affected adjustment. The degree of loss in the total structure of psychological supports, rather than loss in any one area, was critical for functioning. (Dr. Marian Yarrow, NIMH; reported at the International Research Seminar on Social and Psychological Aspects of Aging, Berkeley, Calif.).

Loss of aptitudes in aged

An evaluation of the reasoning processes of the aging individual, made possible through problem-solving experiments designed to identify the processes accounting for failure or delayed success, has provided specific descriptions of some of the mental deficits associated with aging.

In test situations, the aged person was unable to achieve a clear identification of the goal of the problem before embarking on random trial-and-error exploration. College freshmen and sophomores, on the other hand, did not manifest this deficiency to a serious degree on any occasion, whereas all old subjects exhibited it on some problems and most old subjects were frustrated or impeded by it on all.

A lack of organization in search for clues or helpful information was also evidenced, as well as excessive redundancy and repetitious eliciting of the same items of information. Other peculiarities of the aged person's performance included failure to develop strategies, apply those suggested to him, and draw appropriate inferences. The results of the study emphasize the urgency of investigating the feasibility of retraining in the basic heuristic processes which appear to deteriorate so sharply in the process of aging. (Dr. Edward Jerome, NIMH; reported at the International Research Seminar on Social and Psychological Aspects of Aging, Berkeley, Calif.).

Styles of life and successful aging

An intensive study of data on some of the 20 aged persons in Kansas City has been conducted in an effort to delineate various styles of life found among older people and to evaluate the degree of successfulness with which these individuals cope with aging. In the process of studying these cases, a means of defining how successfully an individual ages has been developed which involves a new approach to analysis of the data procured.

The approach is based on observation of the social system in which a given individual functions—the dimensions and structure of his social life space, his modes of interaction within it, his attitude toward it, the satisfaction it provides, and its degree of stability over a period of time. Evaluations are made of two aspects of the social systems of the individuals studied. One concerns the amount of "output" or work a person contributes to the system, and how much "input" or work of others it takes to keep him going. If there is a balance on account, or a plus value on the output side the individual is said to be autonomous; but if it takes more energy to maintain him than he puts out for the system he is said to be dependent. The other aspect of the individual social system to be judged in defining the success or lack of success of an individual in coping with aging is its probable future course. Will it persist, change, or collapse—in short is it regarded as persistent or precarious?

Utilizing these four characteristics, and the relative degree to which they apply to an individual, a judgment can then be made regarding the extent to which aging can be regarded as successful. Four combinations are possible: Autonomous-persistent (successful aging) ; autonomous-precarious (potentially unsuccessful aging) ; dependent-persistent (semisuccessful aging) ; and dependent-precarious (unsuccessful aging).

Through this method, cases can be ranked within each of the four categories. The extreme cases of unsuccessful aging would lie outside the four categories, and would be exemplified by institutionalization or suicide.

This approach to measuring the success with which people age does not involve such factors as the happiness of the subjects or the amount of satisfaction they draw from life.

Determinations of the autonomy-dependency of a social system of an individual, while complex, are made solely on the basis of the subject's social system and without regard to his health or economic status.

This method of determining the extent to which an individual may be aging sucessfully is independent of any specific theory of aging, but it provides a useful frame of reference in exploring varied aspects of theories of aging (Dr. Richard H. Williams, NIMH Professional Services Branch; reported at the International Research Seminar on Social and Psychological Aspects of Aging, Berkeley, Calif.).

Life satisfaction and successful aging

Two indexes of life satisfaction which can be used to measure success in aging in terms of the degree of satisfaction a person feels with his present and past life have been developed by the team involved in the Kansas City study. Preliminary use of these indexes, which show promise of wide applicability, suggest that life satisfaction is positively related to activity for some types of people but is related to disengagement for significant numbers of others (NIMH grantee Dr. Robert J. Havighurst, University of Chicago; reported at the International Research Seminar on Social and Psychological Aspects of Aging, Berkeley, Calif.).

Age and intellectual functions

Investigators at Fordham University have been studying the relationships between performance on a test which measures the brain's ability to perceive and discriminate a rapidly flickering light and brain pathology, age, and intellectual functions. The point at which the intermittent light fuses and is perceived as a steady light is designated as the critical flicker frequency (CFF) for any given individual. Earlier invetigators noted that the average CFF of groups with brain pathology is lower than the average CFF of normal groups, and thus CFF has been viewed as a potentially useful indicator of the integrity of the central nervous system. In their work with 50 women residents (ages 74–80) of homes for the aged in New York City, the researchers at Fordham University explored the hypothesis that if there is a correlation between CFF and intellectual functions, the relationship should be evident in old age, and that there should be more pathologically lowered CFF's in old age than at any other time of life. They administered five tests of intellectual function to a selected group of 50 elderly women who were free of eye pathology, and also tested their CFF thresholds. Their findings corroborated the suggested of earlier investigators who worked with a small sample of elderly men. The results of all but one of the tests of intellectual function correlated significantly with critical flicker frequency. Tentatively the investigators ascribe the relationship of CFF and intellectual functioning to reduced central neural efficiency, or "alertness, in old age, which adversely affects both CFF and intellectual functions, more especially comprehension of new ideas and adoption of new work methods. (NIMH grantees Drs. Armand W. Loranger and Henryk Musiak, Fordham University. Reported in the Journal of Clinical Psychology.)

Social isolation in the aged

A scientific exploration of the adverse effects of social isolation among 100 residents of a home for the aged revealed that a lack of prior personal interaction hindered the older individual's adjustment to a new environment. Social isolation was defined as "the absence of role relationships which are generally activated and sustained through personal interaction." The amount of contact with relatives, presence of children, length of unemployment period, and mode of living—i.e., alone or with others—indicated the degree of withdrawal. In addition to having difficulty in adjusting, the "isolates" appear to have a disruptive effect upon their new surroundings—especially if the social system involved is highly integrated. The most important factor, the investigators feel, is a loss of social skills and sensitivity to social expectations, leading to disruptive nonconformity. More "isolates" than controls in the study had to be transferred to mental hospitals. (NIMH grantee Dr. Joseph Zubin, Columbia University. Reported by Nechama Tec and Ruth Granick in Social Problems.)

Delinquency

Research on prevention

The growing rate of juvenile delinquency, which doubled during the years between 1948 and 1958, has focused alarmed attention on this problem area. With the child population estimated to increase 50 percent in the next two decades, understanding of the factors contributing to juvenile crime and the development of measures to deal with them have become matters of paramount importance to society. The problems are of particular relevance to the field of mental health. Through this strategic discipline, knowledge of many areas may be brought together to be related, tested, and applied.

The NIMH therefore includes this problem among its areas of concern, and during the past year has engaged in and supported numerous research programs designed to provide better understanding of the processes that produce delinquent behavior. While this long-term basic research moves forward, steps have also been taken to increase the effectiveness of community agencies in handling mental and behavioral problems.

Community projects

The elements of an effective prevention and early treatment program on a communitywide or high delinquencywide area have long been recognized. To make immediate inroads on this problem, the Institute has therefore supported several such trial programs designed on a sufficiently extensive basis to produce conclusive results. Emphasis has been placed on development of instruments for early identification, careful recording, classification for treatment purposes, and finally, for evaluation.

New York's Lower East Side, whose underprivileged homes produce a disturbingly high number of juvenile delinquents, is the target of the pilot phase of a demonstration project started this year. The project seeks to explore new patterns of services in a circumscribed area which will affect delinquency. How can the families be reached? To what influences will youth respond? New methods of intervention and modes of management, utilizing indigenous value systems and aspirations, are being utilized. How can potential delinquents be identified at a sufficiently early age so that skilled clinical and social services may be brought to bear, in time? With the cooperation of school personnel in the pilot area, measures which are capable of detecting a percentage of children with a high potential for psychosocial disturbance in early childhood will be utilized. Agencies of the Lower East Side Neighborhood Association in cooperation with Columbia University are collaborating in the project, known as Mobilization for Youth.

A second community project supported by the Institute is underway in Boston. Here methods for classifying a sample of all delinquents coming to court, so as to suggest appropriate disposition of treatment, are being developed by an interdisciplinary team of child psychiatrists, psychologists, social workers, and a social scientist. The project is designed to develop instruments which can be applied by partially trained probation officers or other semiprofessional workers.

New evaluative techniques

Effective evaluation methods are important in early detection of delinquent tendencies. A new technique is now being developed in New York City through Institute support. The method, designed by Dr. Isador Chein, utilizes multiple correlation, with delinquency rates, of a number of factors given by census data for census tracts—such as median incomes, homeownership, racial makeup, morbidity rates. Experience has shown that those scoring high on these indices tend to have high delinquency rates. A multiple service saturation-type delinquency prevention and treatment program is proposed for those tracts in which high correlation exists. As controls, census tracts in the city with very similar characteristics will be used. It is assumed that, if the saturation program is successful over a period of years, the correlation between delinquency rates in this area and the background factors should be substantially reduced, since unfavorable environmental conditions would be offset by the project. The correlation, presumably, would remain high in the control areas. This approach has promising implications for sociological studies, for, if successful, it could be applied to any effort to effect change in a community.

SUICIDE

Suicide is a major mental health problem in the United States, as in other civilized nations of the world, with approximately 18,000 people in this country committing suicide each year.

The Institute this year has continued its support of the Suicide Prevention Center in Los Angeles, Calif. This 5-year project utilizes community agencies to obtain referrals of suicidal persons, and public and private facilities in handling the patients. Arrangements have been made whereby the treatment resource reports back to the center on care provided and on the patient's response.

Comprehensive research on suicidal motivations is being conducted at the center, which is unique. The purpose of the project is to develop hypotheses about the precipitating causes of, and treatment for, persons suicidally inclined; to obtain psychological, psychiatric, and environmental data by means of interviewing and testing such persons; to diagnose and refer them for treatment, and correlate treatment data with subsequent records; and to evaluate the effectiveness of methods of treatment used in the community.

In a recently published book "The Cry for Help," the center has described the results of the clinical and research activities of its interdisciplinary staff of therapists and researchers. Work done by the center will help stimulate other communities to establish suicide prevention facilities and encourage additional basic investigations of the cause of, and effective preventive measures against this serious emotional illness.

RETARDATION

IMPROVING ABILITY TO COMMUNICATE

Procedures designed to improve the ability of severely retarded children to communicate have been developed during the past 3 years by the University of Kansas and the Parsons State Hospital. A variety of ways to stimulate language are utilized in this Institute-supported project which seeks to increase the sociability of institutionalized retarded children, who have been isolated from each other and from the world because they are not able to use language effectively.

Trained aids are instructed on communicating with the children and cautioned not to expect too little of them. Children are encouraged to talk by being asked questions requiring more than a simple "yes" or "no" answer. It was found that children responded more to one another than to adults. The value of incorporating a system of rewards to induce the child to conform to the social conversational norm is underscored.

PILOT SCREENING PROGRAMS

Phenylketonuria is an inherited disease traceable to an inborn error of metabolism which results in mental retardation. The disorder is caused by the lack of an enzyme needed to metabolize phenylalanine, an amino acid, into another amino acid called tyrosine. As a result, abnormal amounts of phenylalanine accumulate in the blood and urine. Although there is no cure for the metabolic defects, it is now known that retardation can be prevented if a special low phenylalanine diet is instituted early in infancy. Findings have shown that treatment must be started in many case as early as at age 4 to 6 weeks if it is to be fully effective. Early diagnosis is therefore crucial.

A pilot case-finding project, made possible by an Institute grant, is now underway in the Cincinnati area to screen infants for evidence of this and other metabolic diseases. Based on a diagnostic evaluation survey conducted as part of this project, it is estimated that the incidence of phenylketonuria is one in every 10,000 newborn children. The program utilizes a diaper test adaptation of the standard urine test. Small squares of filter paper are distributed by hospitals to mothers of newly born infants, with instructions that they be placed in diapers when the babies are 4 to 6 weeks old. When dried, the squares are returned to the hospital, where they are analyzed for detection of phenylketonuria, galactosuria (a disorder resulting from an inherited inability to metabolize galactose and lactose normally), and other patterns of aminoaciduria that may result in mental retardation. (NIMH grantee Dr. Helen K. Berry and associates, Children's Hospital Research Foundation and Department of Pediatrics, University of Cincinnati College of Medicine. Reported in Cincinnati Journal of Medicine, "Clinical Chemistry and Metabolism."))

A similar early detection program in Los Angeles is attempting to establish the efficacy of the filter paper test in early infancy so that the method can be used routinely. These investigators report that in treating the phenylketonuric patient by diet, the physician is faced with the problem of controlling the diet as carefully as he would for the diabetic patient. They also advise frequent testing of urine and blood for the presence of high amounts of phenylalanine since the actual amounts of phenylalanine required to maintain normal blood levels in the phenylketonuric patient appear to vary with each patient. (NIMH grantees Drs. W. R. Centerwall and P. B. Acosta, College of Medical Evangelists, Los Angeles. Reported in the Journal of the American Dietetic Association.)

Retardation and fetal development

Disorders which are associated with mental retardation and which occur during fetal development are being investigated in research conducted by a team at the University of Michigan. These studies have considerable interest with regard to the prevention and treatment of mental retardation associated with congenital hypothyroidism or cretinism (a disease resulting from a lack of thyroid hormone during fetal development which affects the cerebral cortex, with accompanying physical and mental disorders). Until recently cretinism was not considered to be an important cause of mental retardation. However, studies of inhabitants in an endemic goiter area in northeastern India seem to indicate that it may be much more important than had been suspected. Much of the work of this group has been devoted to examining hypotheses dealing with this disease. For example, they have demonstrated that although antibodies are known to cross the placenta from mother to fetus, autoantibodies present in the mother are apparently not a cause of congenital hypothyroidism in the fetus. Thyroid hormone can be administered to the pregnant mother in extremely large doses without apparent harm to the mother and yet be successfully transmitted across the placenta to be absorbed by the fetus.

In a specific case, a woman who had previously given birth to two cretins was given dessicated thyroid when she became pregnant for the third time to assist the fetus to develop normally. At the birth of this child, tests showed that the child was normal and that normal uterine conditions had been produced by the administration of thyroid to the mother during her term of pregnancy. Further studies showed that a fetus may have temporary hypothyroidism, while in utero, which results in brain damage. After the child is born, his thyroid gland develops normally. Thus, the child will be normal physically but mentally retarded to the degree of the temporary nonfunctioning thyroid during fetal development.

From this research has come not only an increasing recognition of the need for diagnosing and treating congential hypothyroidism early, but the actual beginnings of diagnostic methods for recognizing it at birth or a few weeks afterward. The presence of an umbilical hernia, prolounged cyanosis, or a high birth weight (over 9 pounds) have been found to be indicative of congenital hypothyroidism at birth. Within a few weeks other symptoms are observed, such as feeding difficulty, retarded growth, prolonged icterus neonatorum, and respiratory distress with cyanosis. (NIMH grantee Dr. W. H. Beierwaltes and associates, University of Michigan. Reported in the Journal of the Michigan State Medical Society and the Journal of Clinical Endocrinology and Metabolism.)

DRUG ADDICTION

Addiction and mental disturbance

Significant evidence linking mental disturbance and drug addiction has been found by investigators at the Institute's Addiction Research Center. A recent study of 270 hospitalized drug addicts showed that 95 percent of the patients had personality characteristics associated with sociopathy (constitutional psychopathy). In addition to such sociopathic traits, most addicts also had psychoneurotic, hypomanic (depressed), or schizoid traits. Overt psychoses were rare.

Assessment of these characteristics were based on the Minnesota Multiphasic Personality Inventory (MMPI), a standardized objective test which measures several aspects of personality. All groups showed high elevation on the psychopathic deviate scale, and less than 5 percent of the addicts showed normal MMPI profiles. On the basis of information provided, patients could further be subdivided into three groups, including neurotic, hypomanic, and schizoid. The similarity in the personality profiles of adolescent addicts and adult addicts, as well as the resemblance of the profiles of adolescent addicts to those of nonaddict delinquents, suggests that psychopathology has considerable significance in the etiology of addiction. (Drs. Harris E. Hill, C. A. Haertzen, and R. Glaser, NIMH Addiction Research Center. Reported in the Journal of General Psychology.)

Subjective data on addictive drugs

Evaluation of the addictiveness of new narcotics has generally been based on objective measurements, such as the ability of the new drug to suppress withdrawal symptoms of morphine or to create physical dependence similar to that caused by morphine. Little effort has been made to measure subjective responses, in spite of their recognized importance in causing addiction, since reports from addicts were regarded as unreliable and evaluation difficult. Recent studies, however, at the Institute's Addiction Research Center show that subjective responses induced by opiates can be quantitatively measured. Patients receiving drugs, without knowing their identity, were asked a series of simple questions: Did the drug produce any effect? Was it similar to that of any other drug they could name? Were there symptoms such as relaxation and itching caused by morphine? The subjects also rated the strength of the drug. Answers were found to correlate highly with objective measures of drug effects such as constriction of the pupils and intensity of withdrawal symptoms. (Drs. H. F. Fraser, G. D. Van Horn, W. R. Martin, and H. Isbell, NIMH Addiction Research Center. Reported to the Committee on Drug Addiction and Narcotics of the National Research Council.)

Rehabilitating drug addicts

Progress in the extremely difficult and seemingly hopeless task of socially rehabilitating drug addicts has been made at the Institute's unique Drug Addiction Demonstration Center in New York City. Work with addicts, their families, and various social agencies in the community has helped a number of addicts abstain from use of drugs for increasing periods of time. Referrals have been made to several employment services and families have been prepared to assist the addict in readjusting to normal life.

The demonstration center, established in 1957, is staffed by a director, six social workers, a casework supervisor, and a psychiatric consultant. It has functioned increasingly as an informational and consultative source, answering inquiries from professional and lay persons. It has extended its influence through consultation with community agencies, participation in public conferences and seminars, and membership on committees interested in formulating programs for the management of addiction.

ALCOHOLISM

The use of alcohol is one of many mechanisms that can be employed to cope with everyday problems of living. Its widespread use in our culture and the stress imposed by its misuse have focused increasing attention on the causes of alcoholism and methods of prevention. The search for answers to such questions as why some people are able to drink alcohol socially while others employ it as a means of escape from problem-solving, leads directly into the psychobiological disciplines of mental health.

Last year, a grant was made to the North American Association on Alcoholism Programs (an organization of alcoholism program administrators in the United States and Canada) for the purpose of establishing an independent Cooperative Commission on the Study of Alcoholism. With the recent appointment of Dr. Nevitt Sanford, professor of psychology at the University of California as chairman of the commission, a major impetus has been given the program which will reexamine the problem of alcoholism and develop a blueprint for action by communities.

Meanwhile, scientists at the institute are investigating the psychosocial dynamics of alcoholic disease. Others are approaching the problem of alcoholic addiction through metabolic and biochemical studies, seeking evidence of biological factors that may have a bearing on alcoholism. Discovery of such factors, if they exist, might eventually lead to medication to counteract them.

Alcohol and neurohormone concentration in brain

Although the effects of alcohol on the biological system have been widely observed and measured, little has been known about the precise mechanism through which alcohol acts to bring these effects about. An Institute-supported study, designed to test a number of biological factors as possible somatic traits for chronic alcoholism, has now provided an explanation of how the sedative and hypnotic effects of alcohol may occur.

The investigators have presented evidence indicating that intravenous infusion of two grams per kilogram of alcohol produced depression of both serotonin and norepinephrine levels in the brain stem of the rabbit. The parallel depletion of both neurohormones persisted long after the alcohol had disappeared, an effect which is reminiscent of the action of reserpine. Chronic administration of alcohol for 7 days produced 50 percent decrease in both serotonin and norepinephrine levels in rabbit brain stem.

Scientists previously have suggested that reserpine works through releasing epinephrine and serotonin from storage depots in the brain and that its sedative effect results from the bombardment of central receptor sites by free serotonin. The significant similarity in effect on neurohormones which is produced by alcohol has now caused the investigators to theorize that the sedating and hypnotic effects of both drugs may be achieved through the same mechanism. If verified, this concept would provide a physiological explanation of the well-known mood depression of chronic alcoholics. (NIMH grantees Drs. Deha Gursey and Robert Olson, University of Pittsburgh. Reported in Proceedings of the Society for Experimental Biology and Medicine.)

Delirium tremens

The relationship between the serum magnesium level, delirium tremens, and other alcohol withdrawal symptoms are of vital importance in the treatment of chronic alcoholics. Work done thus far has shown that there is a decreased concentration of serum magnesium in patients with delirium tremens and alcoholic hallucinosis. Whether a serum magnesium deficit results from, or is the cause of, delirium, with its increased psychomotor agitation, disorientation, excessive perspiration, and hallucinosis, remains to be determined. However, the findings in a number of the delirium tremens patients who were studied during convalescence showed that the value of serum magnesium increased in each case without the use of magnesium in the therapy, thus failing to substantiate the hypothesis that a magnesium deficiency exists in alcoholic patients who have consumed copious amounts of alcoholic beverages and who have had a poor or restricted diet. (NIMH grantees J. Mendelson, D. Wexler, P. Kubzansky, H. Leiderman, and P. Solomon, Massachusetts General Hospital, Boston City Hospital, and Harvard Medical School, Boston. Reported in the Journal of Nervous and Mental Disease.)

Etiology of alchoholism

Findings of the genesis of alcoholism have been contributed by a study in which members of the Department of Sociology at Stanford University investigated data which had been gathered on a group of male individuals, both before and after the onset of alcoholism in any members of the group. A longitudinal social study was made of the physiological, psychological, and social characteristics of a group of boys and their families, using a sample of 255 urban, relatively lower class boys who were participants in the Cambridge-Somerville Youth Project. Originally selected and observed in the 1930's, these boys were then traced to adulthood. Twenty-nine of the subjects became alcoholics; the great majority did not. By statistically comparing those who became alcoholic with those who did not, the authors distinguished certain psychological, personality, and family traits that set the alcoholics apart as a distinctive human type in their childhood, long before the onset of their disorder. The major findings indicate that the alcoholic had undergone a variety of frustrating experiences. He was more likely to have suffered from various neurological disorders, and more likely to have been raised in a family disrupted by a high degree of conflict and basic disagreement. NIMH grantees W. McCord and J. McCord, Stanford University. Reported in Origin of Alcoholism, Stanford University Press.)

THURSDAY, MARCH 23, 1961.

NEUROLOGY AND BLINDNESS ACTIVITIES

WITNESSES

DR. RICHARD MASLAND, DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. LUTHER L. TERRY, SURGEON GENERAL

HARRY L. DORAN, CHIEF FINANCE OFFICER

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	2,261	3,126	3,446
	Positions other than permanent	182	236	246
	Other personnel compensation	77	82	76
	Total personnel compensation	2,521	3,444	3,768
12	Personnel benefits	138	208	226
21	Travel and transportation of persons	240	244	255
22	Transportation of things	52	50	52
23	Rent, communications, and utilities	75	76	76
24	Printing and reproduction	66	30	30
25	Other services	689	660	685
	Payment to "National Institutes of Health management fund"	2,877	3,184	3,488
26	Supplies and materials	304	427	471
31	Equipment	251	286	450
41	Grants, subsidies, and contributions	32,953	40,253	39,978
	Subtotal	40,163	48,859	49,476
	Deduct quarters and subsistence charges	11	10	10
	Total obligations	40,152	48,849	49,466

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	418	507	560
Full-time equivalent of other positions	16	25	27
Average number of all employees	383	479	534
Number of employees at end of year	438	561	619
Average GS grade	6.7	7.1	7.2
Average GS salary	$5,727	$6.342	$6,384

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(*a*) Research	23, 581	30, 823	31, 152
(*b*) Fellowships	536	980	980
(*c*) Training	8, 888	8, 450	7, 846
Total, grants	33, 005	40, 253	39, 978
2. Direct operations:			
(*a*) Research	6, 137	7, 208	8, 081
(*b*) Review and approval of grants	843	1, 026	1, 051
(*c*) Training activities	37	46	50
(*d*) Administration	203	274	306
Total, direct operations	7, 219	8, 553	9, 488
Total program costs	40, 224	48, 806	49, 466
3. Relation of costs to obligations:			
Costs financed from obligations of other years, net (−)	−73		
Obligations incurred for costs of other years, net		44	
Total obligations	40, 152	48, 849	49, 466
Financing:			
Comparative transfers to other accounts	97	191	
Unobligated balance lapsing	1, 239	560	
New obligational authority	41, 487	49, 600	49, 466
New obligational authority:			
Appropriation	41, 487	56, 600	49, 466
Transferred to "Construction of mental health-neurology research facility" (42 U.S.C. 292)		−7, 000	
Appropriation (adjusted)	41, 487	49, 600	49, 466

Mr. FOGARTY. The committee will come to order. Doctor, do you have a statement for the record?

GENERAL STATEMENT

Dr. MASLAND. I have a statement for the record.

(The statement follows:)

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES

Mr. Chairman and members of the committee, it is a pleasure to appear before this committee to review with you the research and training developments of the past year directed toward the prevention and cure of neurological and sensory disorders.

In this concerted attack against neurological disease, we have attempted continually to define the areas of need and of research opportunity, to find new clues through research, and to recruit and train the scientists who are needed now and in the future to fill our research needs. Progress has been made and the year has brought a number of significant advances in our knowledge of a number of the diseases of great concern to all of us.

RESEARCH PROGRESS

There has now been further clarification of the processes underlying the formation of blood clots in the vessels of the brain which are responsible for certain forms of stroke. The "transient ischemic attack," a frequent forerunner of stroke, which is characterized by transitory neurological dysfunction, is the result of arteriosclerotic narrowing of one or more large vessels supplying the brain. These minor episodes, as well as the stroke which they presage, may be reduced by the use of anticoagulants. In certain cases, surgical removal of the affected vessels appears to offer a cure.

There has been further elucidation of certain diseases responsible for mental retardation. Additional new forms of inborn chemical disorders have been demonstrated, and for one (maple sugar urine disease) a promising dietary therapy has been developed. Chromosomal defects have also been found in a number of forms of mental retardation in addition to Mongolism.

The possible role of an "autoimmune" process in multiple sclerosis and other demyelinating diseases is still uncertain. However, liquefaction of the myelin sheath, a characteristic feature of the disease, has now been observed under the microscope in tissue cultures of nerve cells treated with specific immune serum. Modification of the "allergic" reaction in animals has been achieved by a special desensitization process.

The perennial question of a possible virus agent as a cause of multiple sclerosis has again been raised as a result of the discovery of infectious diseases in sheep and goats which resemble multiple sclerosis and are characterized by latent periods of as much as several years after infection.

Further clues regarding the chemical basis of some forms of Parkinsonism have been developed as a result of the discovery that certain tranquilizing drugs may produce transitory Parkinson-like symptoms. The enzyme systems which react with these drugs have now been shown to relate to manganese—an element long known to cause fatal Parkinsonism.

Migraine headaches have been shown to be associated with the liberation of vasomotor enzymes in the affected areas. A new drug with blocking effects offers promise of relief.

There have been several advances in our knowledge of neuromuscular disorders. The chemical basis of one baffling form of muscle disease—familial periodic paralysis—has now been established. In respect to myasthenia gravis, a new drug (galanthamine) may prove a useful addition to our means of control of paralysis.

Evaluation of diagnostic tests for glaucoma reveals that the tonographic test has distinct advantages for detection. Further advances relating to glaucoma have been made in understanding the disturbances of fluid production in the eye which influence the internal or intraocular pressure. In the evaluation of therapy for uveitis, the use of pyrimethamine has been proven effective in 43 percent of cases when the eye inflammation was caused by toxoplasmosis.

Continuing advances in the surgery of the ear are producing more effective relief for otosclerosis and for certain forms of vertigo. New diagnostic tests, which include actual recording of the electrical responses of the human ear, are now proving capable of clarifying the basic defects underlying hearing and language disorders. These tests point the way for greatly improved educational and training programs.

In addition to these specific research advances, Institute research has moved forward in a number of disease areas: epilepsy, cerebral palsy, mental retardation, multiple sclerosis, amyotrophic lateral sclerosis, muscular dystrophy, and Parkinson's disease. Details of these developments will be made available to the committee.

During the year, the Institute has also recognized certain particularly critical areas of need and has placed special program emphasis on them. These include cerebrovascular diseases, disorders of vision, neurological disorders of childhood, speech and hearing disorders, evaluation of therapy, and instrument development.

CEREBROVASCULAR DISEASES

Working closely with the Heart Institute in this general area, this Institute has focused attention on the need for more precise knowledge of the relationship of disturbances of cerebral circulation to neurological symptoms and for a critical evaluation of medical and surgical therapy.

Research progress and future needs relating to vascular disorders of the brain were outlined by international authorities in April of 1960 at a conference supported by this Institute and organized by the American Academy of Neurology. A summary of major conclusions, prepared by a small group of consultants immediately after the conference, clearly delineated special areas of research need and crucial, unanswered questions. This summary received wide circulation.

Another conference in January of 1961 reviewed subsequent data, which included new methods of evaluating the adequacy of circulation through the brain by the use of radioactive tracers and the refinement of angiographic techniques for determining the location of obstructions of the arteries to the brain. Meticulous studies were presented showing anatomical status of the blood vessels of brains of patients dying from cerebrovascular diseases. These studies provided further information regarding the frequent location of obstructive processes and clarifying the dynamic changes that relate to the sudden occlusions of these blood vessels resulting in stroke.

The final part of the conference was concerned with a review of Institute-supported studies regarding the role of anticoagulants in cerebrovascular disease. Research in this area is being carried forward with increasing momentum. The two cooperative Institute studies are providing a continuing stimulus and important basic background data on the natural history of cerebrovascular diseases and their response to treatment. Studies to date indicate that anticoagulant therapy, though hazardous, can delay the occurrence of strokes in selected cases. Continued studies of these groups are defining with increasing precision those cases suitable for therapy. Additional forms of treatment must also come under investigation in the near future.

Our committee of consultants is continuing to survey this field and is preparing an additional detailed status report for further guidance.

Stemming from heightened recognition of this important field, applications have been received by the Institute for the development of research centers focused on the problem of cerebrovascular disease. The opportunity to mount these broad, interdisciplinary attacks within the center program should initiate significant research.

DISORDERS OF VISION

The opportunity to expand research in problems of normal vision and diseases of vision is making possible specific control of some causes of blindness. The Institute-supported cooperative study continues to seek better methods of screening and diagnosing glaucoma. A glaucoma family study by Institute grantees proves the heavier incidence of glaucoma among relatives of those already diagnosed. Also, a heavier incidence of glaucoma in persons with diabetes has been found. Another investigation showed that persons known to have glaucoma provide an especially fruitful survey group for diabetes. The conclusion is that persons with either glaucoma or diabetes should be tested repeatedly for the other controllable ailment, and should advise all relatives to be checked regularly for both diseases.

A May 1960 conference sponsored by Institute grants brought 34 participants from many fields to confer on diabetic retinopathy. Diabetics are living longer; diabetic retinopathy, which already accounts for 8.4 percent of all blindness, can be expected to increase until controlled by research discoveries.

A new approach to the baffling problem of uveitis, a major blinding disease, is a pilot study for analyzing records of uveitis patients. Initiated at an Institute-supported conference on uveitis, the pilot study may provide clues to causes, prevention, and cure. Successful treatment is reported in 43 percent of the large number of patients referred to the Institute with uveitis caused by toxoplasmosis infection.

NEUROLOGICAL DISORDERS OF CHILDHOOD

Another major program concern of this Institute is the neurological disorders of infancy and childhood. These disorders include cerebral palsy, mental retardation, congenital malformations of the nervous system, and congenital blindness and deafness. Approximately 25 percent of the Institute's research appropriation is devoted to this area, the major focus of which is centered upon the collaborative project. The project recently completed its second year of operation, after 2½ years of intensive preparation. About 5,500 expectant mothers and 4,500 babies were studied in the pretest phase, and as of December 31, 1960, approximately 13,500 expectant mothers and 8,000 babies had been enrolled in the main phase of the project.

The project will eventually involve some 50,000 expectant mothers and their children from all parts of the Nation. Recordkeeping begins in early pregnancy and continues through labor and delivery into the early years of the lives of the children.

Working on the project, at 15 private medical institutions across the country, are obstetricians, pediatricians, neurologists, and specialists in at least a dozen other medical and related scientific fields. All of them have a common goal: to gain new knowledge about the relationship between events and circumstances of pregnancy, labor, delivery, and the first month of life on the one hand, and the later occurrence of neurological or sensory disorders on the other. Their common hope is that this new knowledge will make it possible to prevent these disorders and thereby enable every child to lead a full and useful life.

During 1960, developments of the project included the revision of examination forms and manuals to further assure uniform collection of data on study mothers and babies; the development and adoption of methods for postmortem examination of all abortions, stillbirths, and children dying in the first month of life; and the final preparation for the routine screening to begin in 1961 of blood samples from study mothers during pregnancy for evidence of virus infections.

Only the most fragmentary clues are as yet available from the preliminary analysis of the early data now in hand. Information based on data submitted by the collaborating institutions indicates that the number of study children born with a neurological defect may be much higher than originally expected. A recent check of all data presently available on study children who have had a 1-year neurological examination showed an incidence rate of one cerebral palsied child out of every 100 study children, or 1 percent. The original estimate, based on data from other studies, was one-half of 1 percent.

A serious problem relating to the conduct of research with severely neurologically damaged children results from the fact that many of them are under custodial care in isolated institutions for the retarded. This year, the Institute has organized a survey group to help plan and recommend means of strengthening research activities in such institutions.

In addition to and paralleling the collaborative project, the Institute has an active program of intramural research relating to mental retardation and other neurological and sensory disorders of infancy and childhood. This intramural program is underway at the Bethesda laboratories and in Puerto Rico.

The Institute's Laboratory of Perinatal Physiology in Puerto Rico was established specifically to study perinatal factors leading to cerebral palsy and other neurological defects, and to observe under laboratory conditions the development of the nervous system of both normal and defective animals.

The initial objective to ascertain the role of asphyxiation in producing neurological disorders is being approached. Infant monkeys asphyxiated and resuscitated at birth have been found to develop all degrees of neuromotor and psychological handicaps, including syndromes resembling cerebral palsy, epilepsy, deafness, and mental retardation.

Recent investigations have included the study of the pattern of pathological changes demonstrable in the brains of asphyxiated monkeys. Behavioral tests have revealed abnormalities in normal-appearing monkeys deprived of oxygen at birth, and considerable information on normal physiological values in these monkeys has been collected and analyzed in preparation for further investigations.

New objectives of the project are first to standardize the physiological conditions during asphyxia and to measure damage under agreed criteria, and then to seek means of preventing nervous system damage by introducing certain therapeutic measures.

At the Institute's Bethesda laboratories, research projects in this area include microscopic and chemical studies of the brain and central nervous system. Also, in the neuropathological laboratories, various studies concern close and microscopic examination of the brains of children and adults known to have suffered from mental retardation. These observations in adults and children are being paralleled by animal experiments in which deliberate efforts to produce a mentally retarded animal have been undertaken.

Within the extramural program, grant-supported prjoects include studies on the chromosomes of Mongoloids, the toxic and metabolic deficiency disorders, certain developmental defects, and other studies relating specifically to mental retardation and cerebral palsy. Other investigations relate to asphyxia and lesions of the brain, tests of mentality, and mental development of premature infants who became blind with retrolental fibroplasia before the means for its prevention was discovered.

DISORDERS OF SPEECH AND HEARING

Until recently, our ability to deal effectively with disorders of hearing and the closely associated defects of language was hampered by the lack of accurate diagnostic tests. Lack of comprehension due to deafness from ear disease has been extremely difficult to differentiate from inability to comprehend because of a defect of the central receptive mechanisms. This diagnostic difficulty has been a major obstacle to a clear understanding of the causes of language dysfunction and to the development of effective treatment and training programs.

Highly specialized tests in medical audiology now are solving the problem. The Institute's program has emphasized the training of scientists capable of developing and administering these new tests. The program has also included the application of these tests to the screening of large numbers of normal and handicapped individuals.

Preliminary findings of a survey of hearing and hearing loss in 4,000 schoolchildren have been reported in a large-scale, jointly supported study which shows promise of future important results. One result of this project has been the demonstration that audiometric testing alone cannot identify those physical abnormalities of the ear which may have predictive value in indicating hearing loss.

Similar studies of childhood hearing loss are being conducted by some States. For example, hearing tests of some 11,000 schoolchildren in Nebraska revealed that about 6 out of every 100 children had hearing problems. Although the difficulty of detecting hearing loss in infants has been a major obstacle, recent results indicate that the electroencephalograph may be a useful tool, since responses to sound can be determined by brain wave recordings.

A newly developed technique is making it possible for the first time to record from the human ear and auditory nerve electrical responses to sound. There is thus available a truly objective measure of "hearing" at this most fundamental level.

Through animal experimentation investigators now can trace the sound impulse from the ear throughout the brain. They can observe the modifications of this impulse at the various way stations within which it is "evaluated" by the brain.

Further evaluations of new techniques cited last year for relieving otosclerosis, an important cause of deafness in older age groups, have continued this year. Numerous supported studies report a high degree of success with techniques to restore some hearing by bypassing the rigid middle ear bones with plastic or metal prostheses. However, more experience with these methods is still necessary to adequately evaluate them. In addition, an improved technique for vein graft closure of eardrum perforations has been developed, which may permit simpler, permanent repair of extensive eardrum damage. A surgical means for relieving the majority of severe cases of Meniere's disease was evaluated this year with considerable success.

Complex basis studies of auditory pathways have continued to progress during 1960. In one such project, investigators have utilized the electrical responses of single cells to noise to determine an integrative mechanism of cellular substations along certain nerve pathways.

EVALUTION OF THERAPY

As research in neurological and sensory disorders has advanced during the last decade, many new drugs for the treatment of these disorders have become available. Unfortunately, there has been no corresponding carefully planned evaluation of the results of the use of these drugs.

For example, at one time, having diagnosed a case as epilepsy, a physician decided between bromides and phenobarbital. Today, he finds that there are 15 to 20 standard drugs for epilepsy and another 8 or 10 in the experimental stage. Many doctors believe it is not now a choice of one of these but rather a multiple use of several of these drugs. Other disorders present similar problems of drug evaluation.

In an effort to clarify this entire area, the Institute last spring sponsored a symposium on the evaluation of drug therapy for the treatment of neurological and sensory disorders. In addition to a general session which considered methods of designing clinical trials for therapy evaluation, eight panels of well-known scientists considered the specific problems relating to particular disorders. These panels were on epilepsy, multiple sclerosis, vertigo, headache, diseases of the muscles, glaucoma, Parkisonism and diseases of the basal ganglia, and neuropathies and neuralgias.

The panels are continuing their work and several of the groups have made considerable progress. In epilepsy, the panel has worked out a method of classification of cases and a preliminary form for use in a statistical analysis of results. The various drugs must be evaluated over a period of time with many patients to determine their effectiveness, toxicity, and total bodily effect in relation to each of the many types of epilepsy.

The panel on multiple sclerosis has a particularly difficult task since this disorder has an unpredictable course. It is subject to spontaneous remissions with apparent "cure" but later recurrences. Although no effective therapy is presently available, frequent claims of beneficial results, often made on the basis of unsound data, lend urgency to the development of a sound and agreed-upon program for evaluation. The panel therefore is working to establish guidelines for the testing of therapy for multiple sclerosis. These guidelines will delineate rigid criteria for case selection and for the evaluation of improvement.

The problem of a proper evaluation of the drugs available for the various types of headaches is monumental. It is estimated that several hundred drugs have been put on the market in the last 25 or 30 years for migraine headache alone. One headache clinic is now testing 23 new drugs for migraine and has turned down many others. The remedies have increased tenfold in recent years.

Here too, problems of classification and evaluation are very difficult. Scientists in various areas of the country reporting results of therapy find their work often cannot be correlated with other research because of the lack of uniform procedures. Therefore, the panel on headaches has set three goals, the first of which is the preparation of a uniform descriptive classification of types of headache. The second goal is the preparation of a specific design for drug evaluation studies. The third goal is considered the most difficult—the discovery of specific chemical or physiological diagnostic criteria. The panel believes the first two goals can be achieved during 1961.

Over the next year it is anticipated that the activities of these several panels can have a major influence in bringing order to the present chaos of drug evaluation in relation to these and other important neurological disorders.

BROADENING THE BASE FOR NEUROLOGICAL RESEARCH

Increasingly, neurological research is coming to depend upon long-term projects requiring the use of complex equipment and involving a variety of technical skills. Such projects can evolve only upon a base of broad continuing support. As a participant in the new NIH program of clinical center grants, the Institute is offering support to medical institutions (1) engaged in a multidisciplinary attack on specific diseases of importance in the neutrological and sensory field or (2) engaged in a disciplinary attack on a group of neurological and sensory disorders. This support is for setting up patient beds and providing the salaries of key staff for such centers.

Under the clinical center grants program, we will be particularly interested in such specific problem areas as epilepsy, cerebral palsy, multiple sclerosis, cerebrovascular diseases, disorders of vision and hearing, and neurological diseases of infancy. Fourteen such grant applications have been received and will be reviewed at the next meeting of the Institute's Advisory Council.

Currently being considered is the possibility that this program eventually might provide a mechanism by which regional, multiinstitutional clinical research centers could be developed. At such centers, outstanding investigators from medical institutions in a specific area could utilize necessarily complex and highly expensive facilities for research—facilities which would not be feasible for an individual institution.

Not a part of the clinical center program but of a similar nature is a broad-scale project in neurophysiological research at the University of California at Los Angeles, supported by a large Institute grant. This project, being undertaken by the university's Brain Research Institute, will examine neurochemical and neuropharmacological phenomena in patients selected primarily from those suffering from Parkinsonism and other hyperkinetic disorders, intractable pain, mental disorder, epilepsy, and protracted psychosomatic disorders. It is anticipated that the program will result in the development of improved methods of treatment, greater understanding of the nature of behavioral and medical disorders, and expanding insight into the mind-brain relationship.

TOOLS FOR RESEARCH

Of particular concern in neurological research is the need for the development of highly specialized instruments. This year, two projects have received consideration. One relates to the development of a research center within which highly developed computers will be used for the analysis of the activity of the nervous system. Such computers will be essential to a further understanding of the complex interactions of neuronal pathways within the brain. The second is for a special microscope designed for the automatic counting and analysis of nerve cells seen in microscopic preparations of brain sections. Such an instrument is essential in estimating the billions of nerve cells that lie within the brain. Such projects which rely heavily upon the technical knowledge and specialized skills of the industrial scientists have much to offer to medical research.

TRAINING FOR NEUROLOGICAL RESEARCH

The lifeblood of research is the flow of young, well-trained investigators into its stream. No aspect of the Institute's program can outweigh training in ultimate significance to the cure of disease. Although the total manpower involved in this program remains small, this year has again seen a healthy development in all areas.

During 1960, there were approximately 190 Institute-supported programs of research training in the clinical and laboratory aspects of the neurological, visual, and auditory sciences. New grants approved during the year were for seven new programs in neurological sciences, three new programs in clinical otolaryngology, and two new programs in clinical ophthalmology.

In the development of these new programs, special emphasis has been placed on the neglected field of pediatric neurology and on the basic sciences of neurochemistry, neuropharmacology, and neuropathology. Definite progress can be seen resulting from training in otolaryngology and related fields. Specifically, the number of applicants for special fellowships to further research training is increasing rapidly, and the number of graduates of training programs and the number of special fellows accepting full-time academic appointments are increasing. Also noticeable is an increased number of trainees participating in original investigations—probably one of the most important developments to date.

One immediate major beneficial result from training grants in clinical ophthalmology has been the broadening of basic science training in this field. This leads not only to immediately increased research by members of the training staffs, but augurs well for the training of well-rounded researchers in the future.

During the year, the Institute has provided support for 84 postdoctoral fellows, and 213 special fellows. The latter program, which provides support for the advanced training of highly selected scientists has been particularly productive, with approximately 85 percent of the former trainees now occupying positions in research or teaching.

INTERNATIONAL RESEARCH

In spite of the phenomenal increase in medical research in the United States, which has been brought about to a considerable extent through the programs of the National Institutes of Health, we are still far short of our goal for the elimination of neurological disease and blindness. The accomplishment of this goal will require the recruitment of the most able scientists wherever they may be. For this reason, the Institute has been carefully exploring the research potential of a number of foreign countries in an effort to evaluate their possible contributions. Certain limited support for highly selected foreign investigtaions has now been granted. In general, the grants have been made to selected investigators of unusual ability, and in instances in which a unique disease or geographic situation appears particularly favorable for investigation. Under its regular research grant program, the Institute is currently supporting 36 foreign grants in 19 different countries. These grants are comparable to domestic grants in that they are for independent projects.

The Institute is also supporting one foreign cooperative undertaking—the cerebrovascular study sponsored by the World Federation of Neurology. Additionally, a number of other opportunities for cooperative studies have been suggested. Many of these fall in the broad field of geographic pathology and epidemiology. Studies concerned with the neurological diseases of infancy and childhood are particularly promising. A committee from five European countries is now working on a simplified protocol for a European study to parallel the U.S. collaborative study in this area. And individual laboratories in South America and in certain Asian countries have indicated their interest. Such a study could provide important data relative to the geographic pathology of epilepsy, cerebral palsy, and congenital neurological malformation.

Of particular importance to the international program is the development of the World Federation of Neurology. In 1958, the Institute made a grant to the Federation to support a broad scientific study of the status of international research in neurological and sensory disorders and to discover special research opportunities and needs within this field. The Federation has organized 11 problem commissions, each one concerned with maintaining a broad overview of a special area of neurological research.

The activities of the problem commissions are facilitating a rapid exchange of information, outlining areas of research need, formulating plans for independent and cooperative research undertakings, and indicating the individuals and laboratories through which strong new centers can be developed throughout the world.

Reporting on the whole problem related to Institute-sponsored research overseas is the Institute's Office for International Neurological Research, located in Antwerp, Belgium. Under the direction of Dr. Pearce Bailey, the Institute's former director, this Office for International Neurological Research is performing the vital function of surveying and evaluating international neurological talent and facilities.

PROSPECTS FOR FUTURE RESEARCH

In March 1960, the Institute supported a conference sponsored by the Parkinson's Disease Foundation to review the status of research in Parkinsonism. This conference outlined two fundamental approaches to an understanding of the causes of this disorder: First, a detailed study of the microscopic changes in the brains of patients dying from Parkinson's disease—studies aimed at delineating with accuracy the structures and tissues affected by the disease process; and second, a more accurate knowledge of the chemical structure of those portions of the nervous system which are selectively destroyed by viruses or by specific chemical agents.

The approaches set forth by this conference exemplify the fundamental role which chemistry is assuming in relation to disorders of the nervous system. In the final analysis it is probable that the conquest of the major disease categories in neurology will depend to a large extent upon our ability to recognize and modify derangements of chemistry in relation to the nervous system. For example, the discovery of a basic chemical defect has led to the development of an effective treatment for galactosemia and phenylketonuria. This year the demonstration that still another form of inborn error of metabolism may be influenced by dietary control has been shown.

There are a number of additional disorders affecting the nervous system more directly in which one must certainly give serious consideration to the probability of a basic chemical defect. The muscular dystrophies and familial periodic paralysis are associated with chemical abnormalities. Amyotrophic lateral sclerosis has a specific and symmetrical distribution which strongly suggests a specific chemical anomaly which should be capable of demonstration and control. Chemical abnormalities are evident in the epilepsies, and accurate knowledge of the nature of these anomalies will lead to more specific control than is now available. Important progress is being made in respect to the chemistry of cataract formation in the eye. The retinal degenerations are also a reflection of chemical defect.

With the recent rapid advances in chemical knowledge and technique, the application of this new knowledge to the study of neurological diseases offers a promising challenge. Through a general increase in the study of the fundamental chemistry of the nervous system, together with a broadscale attack from many other disciplines, many new advances should be possible in the next few years.

In conclusion, Mr. Chairman, the amended request for 1962 is a total of $54,100,000 as compared with the adjusted appropriation of $49,409,000 for 1961. This allowance for 1962 will provide for the continuation of the 1961 program levels in all activities and will permit increases in grants for research projects and increases in direct operations. It is distributed among program activities as follows:

Grants:		
Research	$35, 384, 000	
Fellowships	980, 000	
Training	7, 846, 000	
Subtotal, grants		$44, 210, 000
Direct operations:		
Research	$8, 336, 000	
Review and approval of grants	1, 181, 000	
Training activities	50, 000	
Administration	323, 000	
Subtotal, direct operations		9, 890, 000
Total 1962 appropriation request		54, 100, 000

Dr. MASLAND. I certainly wish to thank the committee and my confreres for permitting me to testify at this time. I had made an arrangement to return to be a professor for a day or so, and I would have hated to renege on that opportunity. Visiting universities is one way we can keep in touch with what is going on in the field and actually see how the programs are operated.

If you wish, I might mention a few of the highlights of the program.

Mr. FOGARTY. That will be fine.

Dr. MASLAND. The appropriation last year allowed increases in our grants activity of something over $7 million and pointed out several areas that the committee felt required increased emphasis.

CEREBROVASCULAR DISEASES

The first of these is in cerebrovascular diseases. It was mentioned earlier in the testimony that we have no way of predicting or preventing a heart attack.

It is very exciting to be able to report at this time that in certain types of cerebrovascular disease it is now possible to anticipate the occurrence of a stroke and in certain instances to prevent it.

Several years ago our committee working on the classification of cerebrovascular diseases pointed out a certain type of situation where there were clear-cut evidences of an impending stroke. These evidences consisted of recurrent attacks of weakness and fainting.

Now, with that clue, and using the new diagnostic tests for the demonstration of the arteries of the brain by X-ray, it is possible to observe the vessels on an X-ray film with great clarity—almost as though the skull were transparent, and to demonstrate the locus and existence of a narrowing of the vessels such as would lead to stroke.

In a series of patients with this condition who were treated with anticoagulants, it was conclusively demonstrated that the anticoagulants did stave off the occurrence of the stroke itself, greatly reduced the frequency, and in some instances eliminated these transient episodes of warning.

Mr. FOGARTY. What are some of the warnings of a stroke?

Dr. MASLAND. In these instances, they were transitory neurological symptoms such as a transitory paralysis of some part of the body or a period of loss of speech for 5 or 10 minutes. These things were recurring repeatedly.

They result from an inadequacy of the circulation through a narrowed vessel. When there is a fall in blood pressure or some other change in the dynamics of the circulation, the brain is inadequately nourished for a period of time and the person has a transitory episode.

The other approach to these impending strokes is the surgical one, and I think possibly Dr. Watt may have some words regarding this. Here again, in selected cases, the surgical removal of the damaged vessel in the neck and its replacement by an artificial blood vessel is capable of preventing the stroke. The effectiveness of this has been greatly increased by two technical advances. The first is the X-ray procedure which I spoke of. The other is the improvement in our operative technique whereby hypothermia, that is, the cooling of the body, makes it possible to cut off the circulation for rather long periods of time without damaging the brain.

Advances in the treatability of cerebrovascular disease has greatly heightened the interest of investigators in further work. In spite of the fact that our Advisory Council has had a very rigid standard for all research and has approved only a third of the applications received, we have increased our allocation for cerebrovascular disease by over $1,100,000 this year.

GLAUCOMA

The second area which the committee brought to our attention last year is the problem of the blinding diseases, and particularly glaucoma. Drug therapy for glaucoma is increasingly effective as we become more knowledgeable regarding the mode of action of these drugs and as new drugs with varying effects are developed.

The crucial problem just now is to develop early diagnosis. Unless the disease is diagnosed early and before there has been loss of vision, drug therapy cannot save vision. For this reason we have put considerable emphasis into the cooperative program which we have been developing with the Bureau of State Services for the strengthening and improving of our screening techniques.

One thing which is improving our ability to screen for glaucoma is the discovery that there are certain medical conditions in relation to which glaucoma is more likely to occur. Diabetes is one of these; and certain rheumatic conditions seems to be related to the occurrence of glaucoma. In the general field of diseases of vision, our appropriations in this past year have increased by slightly over $1 million.

MENTAL RETARDATION AND CEREBRAL PALSY

The third area which the committee emphasized has to do with mental retardation and cerebral palsy. Our program including the intramural and the extramural programs in these fields now totals slightly over $10 million a year.

CLINICAL RESEARCH FACILITIES

I would like to say a word about the role of the clinical research facility in relation to neurological disorders. There has been discussion earlier of two types of research centers, the categorical and the noncategorical. Each of these is of very great importance in the activities of this Institute. Let me give an example.

A patient with muscular dystrophy is almost certainly suffering from an inborn error of metabolism; in other words, some abnormality of the chemistry of the muscle. For the study of this chemistry it may be necessary for a carefully selected patient to be admitted to a hospital where he will have a controlled diet, standardized collections of blood specimens and urine samples, and other highly specialized chemical studies.

This can be done very well in a general medical ward—that is, one specifically developed for this type of metabolic study. The patient with muscular dystrophy can be handled there just as can any of the other medical problems. This, then, is the role for the Institute of the noncategorical clinical research center.

On the other hand, consider the problem of the patient with Parkinsonism. Recently there have been developed surgical techniques for the relief of Parkinsonism which involve the insertion of a stimulating or a recording electrode deep within the substance of the brain. In certain instances, this electrode may be left in place for days or weeks, during which time the effect of stimulation or of carefully controlled destruction of this area can be observed. The patient must be watched very closely by people who are especially trained to observe his reactions under these circumstances. Furthermore, the laboratory facilities which relate to this type of activity are highly specialized and are not appropriate to the general research center such as we have previously described. For this type of activity, a categorical research center with a limited number of beds, certainly no more than 5 or 10 beds, and with laboratory facilities directly focused on this type of problem, is most important.

We have established under our regular authority a center in California which has many of the aspects of this type of activity and might in some sense be considered as a clinical research center. Within this center, patients with epilepsy, Parkinsonism, other forms of involuntary movement, and certain mental disorders are being hospitalized in order to be studied by the specialized techniques of neurophysiology.

At the present time we have 13 pending applications for our categorical clinical research centers.

This year we have some interesting information regarding the qualifications of the people who are doing research under the program of this Institute. The outstanding observation is the fact that our investigators are unusually young. A study conducted by the National Institutes of Health of the grantees of the several Institutes revealed the fact that among NINDB grantees almost 40 percent are under 35 years of age. In the NIH as a whole, the percentage is less than 30 percent.

I believe that this is indicative of two important points relative to our training program. First is the serious lack of clinical investigators in the field of neurology which existed prior to the establishment of this Institute and the development of its training program. Second, I think that this evidence indicates that the young men who are being developed from this training program are proving to be effective investigators.

Personally, I am convinced that had it not been for the wisdom of Congress in the establishment of this Institute, and the efforts made by this committee to encourage the development of this training program, the field of neurology would be very inactive and there would only be a few older men like myself trying to keep it going.

THE 1962 PROGRAM

In regard to our Direct Operations, as has been previously indicated, the plans for the new building authorized last year are moving forward. We are even now beginning to recruit the key individuals who will be used to fill in the gaps of the program which are to be rectified by the availability of this new space.

In regard to our activity in Puerto Rico, I believe this activity has demonstrated very forcefully that it is possible to use the monkey for the study of cerebral palsy and mental retardation and the factors which can lead to their occurrence.

The revised 1962 budget provides an increase of approximately $4½ million for extramural research. I would propose to use these funds to extend our program particularly in three areas.

The first of these is in the field of eye research. One of the more common causes of blindness in adults is uveitis, an inflamation of the eye. It has been discovered recently that infection by a small parasite, the toxoplasma, is responsible for about 25 percent of certain forms of uveitis. I am pleased to be able to report that about 40 percent of the group of patients treated with new drugs for this condition have responded favorably.

We need to find the other types of infection, of which there must be several, which are responsible for uveitis. There is a group of investigators planning methods of epidemiological investigation through which further leads to the cause of uveitis can be developed.

The second area of study which I believe we should especially extend is that of epilepsy. We know that 1 out of every 200 people in the United States has convulsions. Actually, we have been amazed to discover that in other countries the incidence appears to be even higher; in some of the South American countries it may be as high as 1 percent. We have a number of new drugs which are increasingly effective for epilepsy. Last spring a symposium, sponsored by this Institute, was held at the University of Wisconsin to develop new methods for the testing of anticonvulsant drugs. The committee which arranged the symposium has continued its progress, and I believe next year we will be prepared for limited field trials for the study of anticonvulsant drugs.

In addition, epilepsy is another disease in which the development of the categorical research center has a very important role. The patient with a convulsive disorder has quite unique problems for investigation—the character of his seizure, his response to anticonvulsant drugs, some of the chemical abnormalities of the nervous system which may be present, and, in certain instances, the response to surgery. We have pending one application for a clinical research center dealing specifically with epilepsy. The proposed budget will make it possible for us to develop broad program projects in this field.

The third area is multiple sclerosis and amyotrophic lateral sclerosis. There are two very important leads which might conceivably lead to an early solution of the problem of multiple sclerosis and I would propose to emphasize the development of these leads in our program next year.

In those instances where critical shortages of trained manpower still exists in the United States with respect to certain highly specialized forms of neurological and sensory research, I would propose to utilize the authority granted under the International Health Research Act of 1960. Through this could be developed carefully worked-out research projects using the skills of a selected group of foreign investigators—investigators who are prepared to work closely with university centers and scientists in this country for an exchange of personnel, ideas, and possibly, even an exchange of equipment. The purpose would be to make the fullest utilization of the best brains around the world to attack the problems of neurological disorders.

I also feel that we must find ways for increasing our utilization of nonmedical scientists in medical research. This probably will involve the improvement of our instrumentation to give stronger and better tools to our research scientists for the conduct of their investigation.

In conclusion, Mr. Chairman, the amended request for 1962 is a total of $54,100,000, compared to the adjusted appropriation of $49,409,000 for 1961. This allowance for 1962 will provide for the continuation of the 1961 program levels in all activities and will permit increases in grants for research projects and increases in the direct operations.

ADEQUACY OF 1962 BUDGET

Mr. **Fogarty.** The appropriation for 1961 is $48,796,500 when adjusted for comparative transfers and nonrecurring expenses. The Eisenhower budget is $49,466,000 or an increase of $669,500. The budget amendment adds $4,634,000 making the total increase $5,303,500.

Now, will you insert that same table and history of your 1962 regular request and the history of the budget amendment that we have asked of the other institute directors?

Dr. **Masland.** Yes, I have it.

(The information requested follows:)

Development of 1962 budget estimates for neurology and blindness activities

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$48,015	−$9,625	$38,390	−$1,417	$36,973	−$5,821	$31,152	$38,472	−$3,088	$35,384
Fellowships	980	+300	1,280	0	1,280	−300	980	1,280	−300	980
Training	10,981	−3,135	7,846	0	7,846	0	7,846	7,846	0	7,846
State control programs	0	0	0	0	0	0	0	0	0	0
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	59,976	−12,460	47,516	−1,417	46,099	−6,121	39,978	47,598	−3,388	44,210
Direct operations:										
Research	10,090	−1,364	8,726	−101	8,625	−544	8,081	8,336	0	8,336
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	1,265	−210	1,055	+5	1,060	−9	1,051	1,317	−136	1,181
Training activities	70	−20	50	0	50	0	50	50	0	50
Professional and technical assistance	0	0	0	0	0	0	0	0	0	0
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	365	−54	311	0	311	−5	306	323	0	323
Total direct operations	11,790	−1,648	10,142	−96	10,046	−558	9,488	10,026	−136	9,890
Total obligations	71,766	−14,108	57,658	−1,513	56,145	−6,679	49,466	57,624	−3,524	54,100

Mr. FOGARTY. Doctor, what do you think you ought to be spending next year?

Dr. MASLAND. Mr. Fogarty, the budget which I have just presented will permit us to continue to develop a strong program and will permit some increases in the special areas which I have indicated.

Mr. FOGARTY. You are not satisfied with that kind of progress, are you?

Dr. MASLAND. I think the problem is that——

Mr. FOGARTY. What did you ask for originally, $71 million?

Dr. MASLAND. $71,766,000.

Mr. FOGARTY. So you must have thought that could be used efficiently, did you not, at the time?

Dr. MASLAND. Yes, sir.

Mr. FOGARTY. You still do?

Dr. MASLAND. Yes, sir.

Mr. FOGARTY. Well, if that is so, then I will answer the question for you. You cannot be very well satisfied with this budget that you have to defend. Neither am I. I will say the same thing about this as I said about mental health. I think it is almost stopping you in your tracks. I do not see much progress in this small increase. About 20 or 25 million people are suffering in the country from neurological disorders?

Dr. MASLAND. It is quite a large figure, yes, sir.

Mr. FOGARTY. This didn't even become a separate Institute until about 1953.

Dr. MASLAND. That is correct.

Mr. FOGARTY. So we have a lot of ground to catch up in neurology. I was hoping that you would take a substantial step forward this time because of this backlog of work in your field. This $71 million that you originally requested, when did you request that?

Dr. MASLAND. This was in the fall.

Mr. FOGARTY. Last fall. I think Dr. Felix said that there have been things that have happened since then and had they known of the recent developments they might have asked for more. Would you?

Dr. MASLAND. No, sir. I believe our estimate last fall would be adequate at the present time.

Mr. FOGARTY. $71 million?

Dr. MASLAND. Yes, sir.

Mr. FOGARTY. What would happen if you got $81 million?

Dr. MASLAND. If we received $81 million we would continue to broaden the program. There are certain areas where we would probably develop some new programs, and it is quite possible that this money could not be spent wisely; if that were the case, it would naturally be returned.

Mr. FOGARTY. You have been in this business a long time now. Do you think $81 million could be expended wisely?

Dr. MASLAND. I believe, Mr. Chairman, that our original request of $71,766,000 is a fund that, in my judgment, could be spent wisely and for a strong program. I think that additional funds beyond that might be spent. I would not wish to guarantee that it could be done wisely.

(More detailed information appears on p. 476.)

Mr. FOGARTY. We would not expect you to expend any funds that could not be spent in a wise and efficient manner.

RECOMMENDATIONS OF THE JONES COMMITTEE

What did the Boisfeuillet Jones report suggest that you ought to be spending in 1961?

Dr. Masland. I do not recall the figure which was recommended by that committee.

Dr. Shannon. Their figures in general were in terms of total rather than specific appropriations, Mr. Fogarty.

Mr. Fogarty. We had it broken down when we went to conference, I know.

Mr. Kelly. The Senate action was the same total amount as the Boisefeuillet-Jones report was by institute, but I do not believe the report was by institute.

Dr. Shannon. That is correct.

Mr. Fogarty. But is it not fair to assume that the Senate committee agreed to those breakdowns and apportionments.

Mr. Kelly. With only minor modifications, the Senate committee——

Mr. Fogarty. It is my understanding that there was agreement with the Jones Committee in the subcommittee, and they said for 1961 you ought to be spending at least $61 million, Doctor, and you are only asking for $54 million in 1962. So you are $7 million and a year behind the Boisfeuillet Jones report?

Dr. Masland. That is correct.

Mr. Fogarty. That is not a very good record. I am not blaming you.

You recommended $71 million originally and still think it could be used. That would be somewhere near the recommendations of the Jones Committee.

USE OF INCREASE IN 1962 BUDGET

Will you supply for the record how the original increase would have been used and then what the effect of the further increase of $4,634,000 will have on your 1962 program? You may supply that for the record.

Dr. Masland. Yes, sir.

(The information referred to follows:)

Effects of increases in 1962 original and revised estimates

Program activity	Increases in original estimates	Additional increases in revised estimates	Total increases in revised estimates
Grants: Research	$329,000	$4,232,000	$4,561,000
Direct operations:			
Research	852,700	255,000	1,107,700
Review and approval of grants	18,000	130,000	148,000
Administration	29,500	17,000	46,500
Total increases	1,229,200	4,634,000	5,863,200

BACKLOG OF GRANT APPLICATIONS

Mr. Fogarty. What will be the total of approved but unfunded research grant applications at the end of 1961?

Dr. **Masland.** It is anticipated that there will be approximately $1,347,000 in approved but unpaid applications for grants; however, if $559,700 in unprogramed funds is returned, this backlog would be reduced to $787,539.

(Note.—This assumes that the institutional grants program will start in 1961. If it does not, it is estimated that there will be no backlog this year.)

Mr. **Fogarty.** Do you think you will have any at the end of 1962 if the present budget before us——

Dr. **Masland.** Yes, sir. According to the present budget, normal program development would involve approved applications for grants of about $4.2 million for which funds are not available.

Mr. **Fogarty.** $4.2 million.

I think that is a pretty good justification for more funds. I think this is an inadequate budget that you are forced to present to this committee.

Mr. **Seggel.** Mr. Chairman, with the release of unprogramed funds in 1961 it will be about $3.7 million.

Mr. **Fogarty.** $3.7 million?

Mr. **Seggel.** Yes, sir; if we get the funds requested this year.

Mr. **Fogarty.** It is still way short of what should be done in this area.

PUERTO RICO PERINATAL RESEARCH PROJECT

I notice you have in the regular budget an increase of $227,000 and 26 positions for your direct perinatal research. How much of this is to be for Puerto Rico?

Dr. **Masland.** $100,000 and 9 positions for a total of $420,000 and 44 positions for 1962.

Mr. **Fogarty.** What do you have in 1961?

Dr. **Masland.** In 1961, we have $310,000 and 35 positions.

FUTURE PLANS

Mr. **Fogarty.** What are your plans for the program in Puerto Rico with regard to expansion, construction of facilities, and location of the laboratory?

Dr. **Masland.** It is our belief that, if this program is to be developed to any extent beyond its present scope, this development should take place within the orbit of the new University of Puerto Rico center and the medical center of the island of Puerto Rico.

Our observation is that this is developing into an effective medical center. A new installation of the Atomic Energy Commission and a new cancer hospital are being built there, and this activity stands to contribute very markedly to the activities of the university and, vice versa, the university, by reason of the personnel who are available, can contribute to the activities of the perinatal laboratory. So it is our belief that if this program is to develop along sound administrative and scientific lines, it should be geographically within the area of this new medical center.

We understand from the dean of the University of Puerto Rico, Dr. Vivas, that land will be available for the activity in that area.

Mr. **Fogarty.** Have you changed your mind in recent months about this, or did I misunderstand you 3 or 4 months ago?

Dr. Masland. That is correct. In respect to the administrative arrangements we feel, for the time being, this activity should continue as a direct operation of the Institute.

We do feel, however, particularly if there should be a desire to expand this activity, that rather than attempting to expand it on the site of the Public Health Service station, it would be preferable for this to be developed within that new orbit which has developed most strikingly even in the last 5 or 6 months.

Mr. Fogarty. I do not know of a better site than where you are right now on the island, as far as accessibility and other factors are concerned.

Dr. Masland. As the new medical center develops at its new location, our present project will be at a disadvantage for it will be operating separately from the new center.

Dr. Shannon. Mr. Fogarty, I do not have the figures here, but as to the medical setup in Puerto Rico it is developing so rapidly that at the present time we are putting about $500,000 in grants for research and about $500,000 in grants for training. The training program has the interesting indirect benefit of encouragement as an area for training of many people who take advantage of the program in being. It draws on all the Latin American countries. Dr. Watt, who will follow, has a good and favorable impression on the development of Puerto Rico as a result of the very extensive visit he made with some of the members of the Heart Council before Dr. Masland and I went down. They are most impressed by the capabilities of this area. We are convinced that this will without any doubt become one of the really effective centers of learning in the Latin American area on its own, staffed by Latin Americans and by Puerto Ricans, and not simply as an aid program depending as a parasite upon continental-developed science.

This is going to be an area for the production of very top-rate scientists. I was tremendously pleased by the progress that the medical school has made during the past year, and by the firmness with which judgments have been reached as to the future of the medical school and the extent to which the legislative group have gone along and provided very broad support. I might say quite out of proportion to what is conventional in many of our States, they are putting a large amount of local funds into this operation and it is within a setting of an understanding ministry of health that goes very well for a total development of really tremendous significance. I was very much impressed by it.

Mr. Fogarty. You must have spent much more time there than I did.

Dr. Shannon. I think Dr. Watt has spent more time than I and has visited not only by himself but with the Heart Council. You may wish to ask him about his reactions.

Mr. Fogarty. How is our friend Dr. Windle? What does he think about this situation?

Dr. Masland. Dr. Windle is very much in accord with this. He has spent the last 4 months at the project in San Juan, and his experiences in this time, in discussing the whole project with the dean of the medical school and other officials, has led him and me to this new concept.

Mr. Fogarty. He must have been brainwashed in the last couple months.

Dr. **Masland.** The crucial issue on which Dr. Windle and I agree is that for the time being this should be continued as a direct operation administratively, but that it should grow into the orbit of the new medical center.

FACILITIES NEEDED

Mr. **Fogarty.** To continue it as a direct operation, then, what additional facilities do we need there?

Dr. **Masland.** It would be as I have indicated earlier. It could be continued at its present level as it now is within the present temporary building.

Mr. **Fogarty.** I thought when we were down there that you thought we needed one or two smaller additions right away. It is very inexpensive construction.

Dr. **Masland.** That is true.

Dr. **Shannon.** I think the problem of putting more money in the PHS outpatient clinic and quarantine station there is that you cannot come up with laboratories that would be adequate to attract a permanent staff. It is a compromise and the facilities are not really topflight. They are very good as temporary facilities and my advice to Dr. Windle and Dr. Masland was not to spend a substantial sum on the present site but to plan a more permanent installation within the scientific environment where as a long-range program this would flourish.

Now, this actually could cause a delay of the program by about a year. But if one made any substantial change in the PHS station really to develop a modern facility there I think work would have to stop for about a year while this was being done because most—much of what was already built would have to be replaced.

Now, the other thing is I don't think that the city of Puerto Rico would look with favor at putting more permanent installations there because we talked to the mayor of Puerto Rico and some of the city fathers. It is quite obvious that in their attempt to rehabilitate Puerto Rico they would like to return this to park space, to historical areas and the like, and they already in fact have moved to take the whole dock area out and put it over on the other side of the peninsula, and the place even were we allowed to stay then would actually be isolated from easy contact with other scientists.

Now, we also spent considerable time looking at the facilities that there are on loan from the medical school in the old buildings of the School of Tropical Medicine in San Juan. I would say if the facilities at the PHS installation are inadequate, these are even more inadequate. They have no outside windows. The monkey facilities are grossly inadequate, and I do not think that there is the basis for a long-term development.

I think that this has been found, that it has demonstrated that there is a role in an area where monkeys can be brought up and observed year-round without the problems of air conditioning and heating. You can have a cage colony that is healthy and do the type of work that has never been done before on this form.

My advice to Dr. Windle and Dr. Masland, I might say, Mr. Fogarty, this was not brain-washing, that they take a hard look at where this program ought to be 5 or 6 years from now and then come up with a program that they could stand solidly behind if they would do it with the means available to me. I would support it.

Mr. FOGARTY. Let me put it this way. They must have been impressed with the speech you made to them before you asked them to look into it.

Dr. SHANNON. No, sir. I think they reached very sound decisions. I might say——

Mr. FOGARTY. Off the record.

(Discussion off the record.)

Mr. FOGARTY. Back on the record.

You have leased two additional islands?

Dr. MASLAND. Yes, arrangements are about completed.

Mr. FOGARTY. When do you expect to get into operation?

Dr. MASLAND. It will be possible for us to have monkeys on the island within a year.

POSSIBLE DIVERSIFICATION OF RESEARCH

Mr. FOGARTY. Are you going to diversify your research at all?

Dr. MASLAND. The main emphasis of the program will continue to be on the perinatal problem, the problems of pregnancy, factors operating during pregnancy and the production of cerebral palsy and mental retardation.

It has been quite evident that the animals may prove to be valuable in unexpected ways.

Earlier in the discussion it was mentioned, for example, that in order to develop an effective measles vaccine it is essential that there be available monkeys with a rather limited exposure to infection.

We have on the island a number of monkeys who were born on that island and have never had exposure to other animals and have had very limited exposure to humans. The likelihood is that these animals would be of unique value in this connection.

There are similar problems related to neurological disorders, and I could go into this if you would like.

Mr. FOGARTY. Yes, I would like to hear from you.

MULTIPLE SCLEROSIS

Dr. MASLAND. There are in fact at least three general neurological disorders where the likelihood of infection is considerable. The first of these is multiple sclerosis. There are peculiar things about the distribution of multiple sclerosis. Multiple sclerosis is almost six times as common in Canada as it is, for example, in New Orleans. It is always more common in the cold climates. It is common in northern Europe, in Scotland. It is very rare in the Tropics. In fact, there is some doubt whether multiple sclerosis is ever seen in Central America. It is not very common in Japan.

Now, there is a very interesting opportunity to study this problem in Israel. Here there is a very strong medical science group and to this country have come people of similar racial extraction from many different parts of the world as part of the resettlement program. The interesting thing is that multiple sclerosis, in persons coming back to Israel from northern Europe, is as common as it is in northern Europe. In people coming from the Orient, it is rather low in its incidence. In the Jewish people who were born and lived in Israel, it is practically nonexistent.

In South Africa there are similar observations. This disease is almost never seen in the African native unless he has been to Europe for a period of several years and returned to Africa. In that event he may develop multiple sclerosis after he gets back home.

Now, this is very difficult to explain. It is hardly likely that this is a dietary problem since the disease may continue to develop in this other environment. It is obviously not a racial inherited condition, and I think there is a strong likelihood that we are dealing here with an infectious process.

If such, it is an infectious process that is not likely to be found in animals; it is like many other diseases where it might grow in monkeys. It is not very likely to grow in mice.

Mr. Denton. What makes you think it is an infection—just because people have it in one country and do not have it in others?

Dr. Masland. This is a distribution which has been seen in certain other infectious conditions.

You do have to assume also some additional contributory factors.

An interesting point in this Jewish situation is that the disease is also seen in the children of Jewish people who have lived in Europe.

Dr. Shannon. The critical point here is that the Africans, for instance, spend limited time in Europe, will return to their home country and then subsequently develop the disease whereas if they do not leave their home country the disease does not develop.

It is things like this together with the experience of children in Israel that Dr. Masland discussed.

Dr. Masland. If mutiple sclerosis is in fact due to a virus, we are dealing with an organism that is going to be very difficult to demonstrate. It will probably grow only in monkeys and will take possibly several years for the infection to become evident.

We have recently had an interesting example of this in a disease that rather resembles multiple sclerosis that has been observed in sheep in Iceland. For a long while this was spoken of as a degenerative or inherited disease, but recently it has been discovered that this is in fact an infection, but it takes 2 years for the infection to make itself apparent after the animal is exposed.

Now, if we are to develop a program which will really decide whether multiple sclerosis is an infectious process, we will have to set up a procedure for obtaining monkeys whose exposure to such conditions has been very limited. These animals will have to be inoculated under carefully controlled circumstances with material obtained at biopsy or by other means. Following this, they will have to be kept under close observation in an isolated environment for a period of several years.

PARKINSON'S DISEASE

Now, the same is true with Parkinsonism. This is the second disease where we have a strong suspicion of a virus. There was an epidemic of sleeping sickness in 1918 and 1920, at the same time as the epidemic of influenza, and this was a very horrible disease. Particularly children affected by this virus became drowsy. They would sleep all day and then they would tear around the house at night. There was a reversal of their sleep ratio. Then, there were violent behavior disorders. These were the most uncontrollable children with which we have had to deal. No management would handle them. And many of these children subsequently developed tremor rigidity and so-called postencephalitic Parkinsonism.

Interestingly enough, children who had a very minor disease at the outset might develop Parkinsonism, 5, 10, or 15 years after the original illness. When I first had my training back in 1935 and 1940, we were still seeing individuals, then adults, coming down with Parkinsonism as a result of this encephalitis which they had when they were children back in 1918 and 1920.

Now, we hope that this virus has died out. No one has ever been able to capture the virus that caused this disease but we know it was a virus. We hope the virus has died out but we have no certainty of it and we still see patients with Parkinsonism—the disease having all the characteristics of this epidemic in 1918.

EPILEPSY

The third entity is certain types of epilepsy in childhood. Recently it has been demonstrated that certain progressive forms of epilepsy in childhood can be attributable to a Russian virus, a Russian spring-summer encephalitis virus. Again it has shown the same characteristic. The child has an initial illness. They seem to get over it and then a year later or 2 years later they develop evidences of continuing infection of the nervous system.

There is now an opportunity to attempt to culture a virus from patients suffering from each of these three diseases. Another clear-cut examples is the herpes virus. Almost everybody in our culture has had herpes at one time or another. Apparently the virus lurks there waiting for something to happen, some lowering of resistance or additional stress. Every now and again somebody comes down with a herpes encephalitis—a fulminating disease which may be fatal. It is quite evident that low-grade virus infections of the nervous system play a definite role in some of our most serious neurological disorders.

PROGRESS IN TREATING CEREBROVASCULAR DISORDERS

Mr. Fogarty. You are making some significant progress in the treatment of cerebrovascular disorders?

Dr. Masland. Yes.

Mr. Fogarty. Do you have anything else you want to add to what you said in your opening statement?

Dr. Masland. As far as future developments are concerned, one of the very encouraging things is the discovery of fibrinolytic agents. These are substances that will dissolve a clot rather than simply prevent its formation. Such substances are now available and they have been proven to be effective in experimental brain clots in animals. Unfortunately, it is my impression they are not yet sufficiently stabilized and consistent in their action. We would not recommend very extensive field trials with humans at this time.

The use of the anticoagulants is rather limited when a stroke is once underway. There is some evidence from our cooperative studies that the anticoagulant does influence the course of the picture even then, but the fibrinolytic agent, which will actually liquefy the clot, has a much better prospect.

Mr. FOGARTY. You mean when these signs develop that you might have a stroke, it is too late to take an anticoagulant then?

Dr. MASLAND. At that point it is useful, but when the person actually starts to have the stroke, the value is limited.

Mr. FOGARTY. I see.

Dr. MASLAND. Of course, even more important than this is the whole question of the prevention of the process, the prevention of the narrowing of the vessel. We are working very closely with the Heart Institute in developing this program and the concern for those facets of it is much more directly in their area. However, there is an opportunity for field trial of diet and certain hormones which seem to influence the atherosclerotic process.

Mr. FOGARTY. What are you going to do about this field trial next year?

Dr. MASLAND. Some such studies are already in progress.

Mr. FOGARTY. Do you think more should be in progress?

Dr. MASLAND. I believe there is an opportunity for——

Mr. FOGARTY. I think we said last year you ought to spend $1 million of the increase over the budget, on these disorders. How much do you think you could use next year?

CLINICAL RESEARCH CENTERS

Dr. MASLAND. I think part of this would depend upon the establishment of additional centers for cerebrovascular disease.

Mr. FOGARTY. What is that?

Dr. MASLAND. I think part of this would depend upon establishment of broad projects and centers for cerebrovascular disease. We have several such applications pending at this time, assuming the approval——

Mr. FOGARTY. Put in the record how many there are and how much they amount to.

Dr. MASLAND. All right, sir.

(The information referred to follows:)

NINDB CLINICAL RESEARCH CENTER APPLICATIONS

The NINDB Clinical Research Center grant program provides a means by which outstanding groups of clinical investigators can devote their efforts to crucial problems in the diagnosis and treatment of diseases of the nervous system, vision, and hearing. Clinical research center grants will usually be awarded to scientists who have already demonstrated their scientific competence and who are able to organize an interdisciplinary, interdepartmental, or interinstitutional clinical research team. The centers will provide for needed clinical studies on a regional basis on diseases such as cerebrovascular disease, epilepsy, glaucoma, and otosclerosis.

At the present time we have the following 13 pending applications for these centers. These are as follows:

Institution	Subject	Amount requested 1st year total
University of Minnesota, Minneapolis, Minn.	Cerebrovascular disease	$640,844
Cornell University, New York, N.Y.	do	219,795
New England Center Hospital, Boston, Mass.	do	123,525
Wayne State University, Detroit, Mich.	do	263,688
University of Iowa, Iowa City, Iowa	Diseases of the eye; neurological diseases	271,825
San Francisco Institute of Medical Sciences, San Francisco, Calif.	Diseases of the eye	267,682
University of Chicago, Chicago, Ill.	Diseases of ear and eye	181,105
Columbia University, New York, N.Y.	Neurological diseases and diseases of muscle.	148,475
Albert Einstein College of Medicine, New York, N.Y.	Neurological diseases including epilepsy and demyelinating diseases.	397,746
St. Joseph's Hospital, Lancaster, Pa.	Neurological diseases of children	180,683
Albert Einstein College of Medicine, New York, N.Y.	Brain damage of children	177,421
University of Wisconsin, Madison, Wis.	Epilepsy	233,142
San Francisco Institute of Medical Sciences, San Francisco, Calif.	Encephalitis	340,999
Total		3,446,930

UVEITIS

Mr. Fogarty. Now, in your research on blindness you told us about your special emphasis on glaucoma but you said in your opening statement that more should be done on the problems of uveitis.

Dr. Masland. That is right.

Mr. Fogarty. What causes uveitis?

Dr. Masland. There are several forms of uveitis; and two mechanisms appear to be active. One is a direct infection of the eye.

Mr. Fogarty. Are glaucoma and uveitis the two leading causes of blindness today?

Dr. Masland. Glaucoma and cataract are the leading causes of blindness. However, uveitis is of very great concern to us. Trachoma is quite important in other countries and we still have a little trachoma in this country.

Mr. Fogarty. Were you going to say something more about uveitis?

Dr. Masland. Some cases of uveitis are the result of direct infection of the eye and toxoplasmosis is one organism. Another organism, histoplasmosis, is probably implicated.

Some cases of uveitis result from inflammation due to some autosensitization process through which the body has developed immunity to its own tissues and actually destroys itself in this fashion. If we can find ways of modifying that reaction there is a good possibility of helping uveitis patients.

AUTOIMMUNE REACTIONS AND MULTIPLE SCLEROSIS

Mr. Fogarty. I believe you said something in your opening statement about one or two leads in multiple sclerosis. Were you referring to this infectious problem?

Dr. Masland. That was one.

Mr. Fogarty. What is the other?

Dr. Masland. The other is again the autoimmune reaction.

Mr. Fogarty. What is that?

Dr. MASLAND. In this situation, an individual develops an immunity against portions of his own body, against specific chemicals which normally should be present in his body. This can be produced experimentally by immunizing an animal. If you inject, under certain circumstances, brain tissue into an animal, that animal develops an immunity against brain tissue and his brain will be destroyed. And the picture has some resemblances to multiple sclerosis.

Mr. FOGARTY. This is more hope than has been given to us in this problem in quite a few years.

Dr. MASLAND. These are very interesting leads.

Mr. FOGARTY. If they are interesting, are you going to double your efforts or triple them or what? I do not think there is anything worse than multiple sclerosis, is there?

Dr. MASLAND. It is a very disabling disease.

Mr. FOGARTY. And fatal in many cases, in most cases?

Dr. MASLAND. That is right.

Mr. FOGARTY. What are you going to do about it next year? You have these two promising leads. I hope you have some really progressive plans.

REPORT ON MULTIPLE SCLEROSIS

Dr. MASLAND. I would be glad to submit a statement on this.

Mr. FOGARTY. I wish you would, because every year we hold these hearings—for about 10 years now—we have not been asking you about progress in this field. It seemed to be at a standstill every year because no one seemed to have any leads. I think, since you do have these leads now, that you should develop for the record a plan as to how much you could effectively use for stepped-up research in this area.

(The report requested follows:)

MULTIPLE SCLEROSIS

THE PROBLEM

Multiple sclerosis is a major disorder of the central nervous system which causes myelin—the fatty, protective tissue sheathing the nerve fibers—to disappear in scattered patches. Lost myelin fails to regenerate when mutliple sclerosis is present and is replaced by scar tissue which distorts or impedes transmission of impulses from the affected nerves to the parts of the body that they control. With loss of conductivity along nerve fiber pathways, motor and sensory disturbances occur.

Young adults between ages 20 and 40 are the chief victims of this mysterious demyelinating ailment which affects an estimated quarter million Americans. The cause of multiple sclerosis and a generally effective treatment are still unknown.

The disorder, chronically progressive in the majority of affected persons, proceeds in a series of unpredictable attacks. In earlier stages, attacks are often followed by periods of remission. With successive episodes, resulting lesions in the brain and spinal cord become more dense and destructive, causing more severe disability.

Multiple sclerosis is essentially a cold-climate disease; it is infrequently seen in the tropics or subtropics. Prevalence is strikingly higher in Northern States of the Nation than in Southern States. Outside the United States, prevalence of multiple sclerosis varies similarly with geographic latitude. Yet no one knows why more cases occur in colder regions than in warmer zones. Once multiple sclerosis has occurred, there is no evidence that a move to a warm climate will control or cure it. In certain tropical areas where the disease had previously been virtually unknown, it is appearing in natives who have returned to these countries after having lived for periods of time in countries where the disease is prevalent.

Diverse theories concerning the possible cause or causes of the disorder have been proposed. These include unknown factors leading to chemical, metabolic, or enzymatic disturbances; an allergic reaction or other sensitivity phenomenon; a virus infection; inadequate blood circulation; a nutritional deficiency; constitutional vulnerability; and other precipitating or contributing factors. Proof is lacking of what internal or external influences actually triggers the onset of the disease, but many investigators are exploring the possibility that a number of factors, perhaps operating as links in the chain of causative agents, are responsible.

RESEARCH ACTIVITIES

Several research-provoking discoveries have been added to earlier reported gains in knowledge of the chemical and physical processes related to the formation and destruction of myelin.

The process of scientific investigations has been hampered by the inability of investigators to produce in animals the exact symptoms of multiple sclerosis. But, within recent years, they have found techniques for reproducing experimental allergic encephalomyelitis, an inflammatory disease of the nervous system which resembles certain human demyelinating disorders and is believed associated with some mechanism of allergic reaction of nervous tissue. New findings are emerging from these studies:

Last year, for the first time, allergic encephalomyelitis induced in guinea pigs was suppressed by administering the same chemical compound which most effectively produces the disease. This important discovery by Institute grantees was a byproduct of experiments designed to test skin reactions of vaccines known to cause encephalitic diseases in animals. The finding suggests that a specific desensitization process may be responsible for the suppression. Further experiments are necessary, however, to explore the possible implications.

In the first tissue culture approach to the experimental study of the same disorder, Institute grantees found that serum from animals with allergic encephalomyelitis can induce nerve demyelination in cultures of newborn rat cerebellum. Direct observation of a tissue culture may supply valuable clues on the underlying patterns of myelin degeneration.

Although liquefaction of myelin in nervous tissue culture can now be observed, the experimentally induced disease, which is created by the injection of brain substance into animals, is still not identical to multiple sclerosis. Thus the problem remains to discover what starts the demyelination process in humans.

Discovery of infectious diseases, scrapie and visna, in sheep and goats which resemble multiple sclerosis and are characterized by latent periods of as much as several years after infection, has sparked renewed interest in a possible virus agent as the cause of human demyelinating disorders.

The theory that human demyelinating disorders may result from an allergic reaction between tissue of the nervous system and certain abnormally produced antibodies has provocative implications. If it should be true that multiple sclerosis is a sensitivity or autoimmune reaction which, in turn, may be stimulated by a latent viral agent, ways must then be found of producing a desensitization through use of drugs or other agents. Current studies may supply links between the experimental condition produced in animals and spontaneous human pathology of the nervous system.

Since clues as to cause may come from knowledge of the incidence of a disease in populations living in different environments studies in the epidemiology of multiple sclerosis continue to be an intensive aspect of research. In the past year Institute investigators initiated studies of the prevalence of multiple sclerosis among ethnic groups in Israel and the incidence of the disorder in American Indians in the upper Midwest and in the Southwestern States Nutritional and other factors which often vary with the geographic and genetic pattern of the disease might have a bearing on the chemistry of myelin.

Neurochemistry studies which seek to fathom the secrets of myelin formation and destruction are becoming increasingly prominent in the laboratories at Bethesda and among grant-supported activities A few of the studies in which investigators are probing the biochemical riddle of myelin relate to chemistry and metabolism and brain lipids antigenic materials in demyelinative diseases, intracellular enzymes in demyelination of nerve, electron microscopy of abnormal myelin, biochemical changes in degenerative nerve, and many others in the chemical and cellular makeup of myelin, its development, and its alterations

A PROGRAM FOR THE FUTURE

Hope of combating multiple sclerosis lies in a vigorous program of research. The Institute's present program is being conducted in three major areas where the application of additional resources may lead to important advances in the future. These areas of investigation relate to:

1. Studies in the nature of myelin and the characteristics of the destructive processes in disease

The growing momentum of research activity to learn what causes the loss of myelin, how this loss can be prevented, and how to restore myelin once it disappears gives good reason to believe that science will find the cause of multiple sclerosis and then the means of eliminating or halting the process of the disease.

Strides are being made in understanding the neurochemistry of white matter of the brain and spinal cord, where the lesions in multiple sclerosis occur. Current biochemical studies of important fatlike and protein substances in the central nervous system and their normal and abnormal metabolism are likely to produce important gains in knowledge of the cause of demyelination.

The Institute's expenditures for basic research in the sclerosing disorders are currently at the level of $1,259,000 a year. An increase to $1,639,000 could be planned in 1962, or about a 30 percent increase.

2. A search for the causative agent in multiple sclerosis

So far, one of the most challenging clues to the cause of multiple sclerosis is its unusual geographic distribution. In October 1960 the Commission on Biometry and Genetics of the World Federation of Neurology reviewed data resulting from epidemiology surveys being conducted in New Castle, England; Iceland; Faroes-Shetland Islands, Scotland; the Hamburg-Cologne-Marseille area; and South Africa. Investigators in these regions confirmed the consistency of the earlier reported variation in the distribution of the disease with climate, and they are proceeding to develop a coordinated plan for worldwide studies. As their objective, these studies will seek to correlate observed variations in the incidence of the disease with more specific geographical variables, such as average temperature, rainfall, diet, exposure to sunlight and radiation, and other living conditions of the exposed populations.

Currently, investigation of the geographic pattern of multiple sclerosis are supported at an annual level of approximately $241,000. Expanded activities of the present group of investigators, coupled with studies by other investigators if their plans materialize, could triple the need for this activity to about $750,000 in fiscal year 1962.

An intensive search for a virus agent in multiple sclerosis is both difficult and costly. This is a complex operation because it is unlikely that a virus for multiple sclerosis would grow well in lower animals, and because there might be a long incubation period between inoculation and development of symptoms.

A successful program geared to the search for viruses would require a supply of specially prepared and selected monkeys, and a facility where these animals could be inoculated, then observed within an isolation unit for periods of time up to several years. Because few investigators have had such animal resources and unique facilities for a virus-testing program, expenditures in this area in 1961 are under $20,000. A broad, effective program for this purpose would involve establishing a limited number of clinical research centers where the work might have to be carried out under contract, or as a direct operation of this Institute. To develop and carry out such a program in fiscal year 1962 would call for an expenditure of $1,500,000, apportioned among grants, contracts, and direct operations.

3. The evaluation of therapy

Ultimate goals are prevention and therapy. Although allergic encephalomyelitis is not identical with multiple sclerosis, it bears many resemblances. Possibly, measures which prevent experimental disorders may also be helpful in alleviating or preventing the human disease. Studies of this phenomenon, now supported at a level of about $180,000 in 1961, could probably increase to $240,000 in 1962.

The unpredictable course of multiple sclerosis makes it difficult and tedious to evaluate the response of this disease to drugs. As new therapies become available, their effectiveness should be rapidly evaluated. At present, a team of investigators is studying methods for drug evaluation in this disorder. Implementation of a broad-scale program for drug testing, both through grants and contracts, would require approximately $500,000 in 1962.

The aggregate proposed expansion in program areas where increased manpower, funds, and facilities may advance research findings in multiple sclerosis is indicated as follows: Estimated funds needed for such a program are included in the professional judgment budget presented by NINDB for fiscal year 1962.

Current and estimated NINDB needs for research in the sclerosing disorders, fiscal year 1961 and fiscal year 1962

Program area	Present expenditure, fiscal year 1961	Estimated need, fiscal year 1962
Basic research	$1,259,000	$1,639,000
Epidemiology	241,000	750,000
Drug therapy:		
Experimental studies	180,000	240,000
Clinical evaluation studies	------------	500,000
Virus testing	20,000	1,500,000
Total	1,700,000	4,629,000

OUTLOOK

In summary, as the base of biochemical studies is broadened, as studies of autoimmune reactions of the organism proceed, as the search for a virus as a causative agent continues, as epidemiology studies provide additional facts, and, most important of all, as more medical investigators, teachers, and other needed personnel enter research, so will the chances of conquering multiple sclerosis grow.

POSSIBILITIES IN TREATMENT OF MULTIPLE SCLEROSIS

Mr. Fogarty. It will be in your report, but tell us a little more now about hopes for people who have this disease.

Dr. Masland. If, in fact, this is an allergic reaction, a sensitivity reaction, then mechanisms for modifying this reaction might prevent the progress of the disease.

Again, in experimental animals, there have been two clues as to how this might be accomplished.

First, by modification of the sensitization procedure by more injections of the causative agent. The body's reaction to that agent can sometimes be further modified into a different type of response.

Another peculiar observation is the fact that animals that are deficient in vitamin C during the time that they should have been developing this disease did not become sick. No one knows the explanation for this, but it indicates that something was capable of modifying the immune reaction of the animal so that he did not develop this autoimmunity.

Now, from the point of view of treatment there are important things that can be done and should be done for the rehabilitation of the patient from multiple sclerosis. This is a disease of recurrence and remissions. The use of physiotherapy, occupational therapy, and retraining often rehabilitate patients with multiple sclerosis for many years.

One thing which is becoming evident is that there are patients who have one or two episodes of multiple sclerosis, who recover from those episodes, and who may never have another one for the rest of their life. This means that however disabled the person may appear to be from multiple sclerosis, an attempt to rehabilitate him should be made.

Every effort should be made to keep him on his feet in the possibility that he may be one of those individuals who may not have another attack.

Mr. Fogarty, it is a fact that we do not have a cure for multiple sclerosis nor do we have a means of significantly altering the course of this disease. There is no cure immediately in sight. These two lines of approach which I have indicated are hopeful lines of approach.

Mr. Fogarty. What about the publicity given to a new drug a short while ago?

Dr. Masland. That was very unfortunate. This is an example of the need for the type of program that we have been developing this year. That is a program for the adequate testing of new drugs for the treatment of neurological disorders.

A small group of investigators which was organized at the Wisconsin meeting last spring is continuing in the development of a program for drug testing. They are working on basic questions such as: "How can you classify your patients?" "How can you be sure this patient is really better? How many patients should be treated before you know that your drug is really helpful?" The committee will be ready to move on this, I think, quite soon.

REHABILITATION OF MULTIPLE SCLEROSIS PATIENTS

Mr. Fogarty. Where is the best place in the country for rehabilitation of people with multiple sclerosis?

Dr. Masland. I would be hesitant to attempt to select any one institution as being the only one or being outstanding.

Mr. Fogarty. I am just trying to get some examples.

Dr. Masland. The most outstanding place is the Institute of Physical Medicine and Rehabilitation of the New York University—Bellevue Medical Center under the direction of Dr. Howard A. Rusk. They have a strong physiotherapy program. Patients are retrained in accordance with the abilities they still have. They are getting many of these people into useful occupations.

Mr. Laird. Mr. Chairman, what about this hospital over in Virginia, just off Shirley Highway?

Dr. Masland. The rehabilitation hospital?

Mr. Laird. Do they take people with multiple sclerosis?

Dr. Masland. I think so.

Mr. Fogarty. That is Dr. Engh in Arlington?

Mr. Laird. Dr. Engh. Have you had any experience with the kind of work they have done?

Dr. Masland. I have not visited that institution, no.

Mr. Laird. I understood they receive Federal funds through Vocational Rehabilitation.

Dr. Shannon. It is a general program and cut pretty much across all important fields.

Mr. LAIRD. Are they limited mostly to orthopedic work?

Dr. SHANNON. I do not believe so, sir.

Mr. KELLY. There is a heavy emphasis on orthopedics.

Mr. FOGARTY. Is there anything else you want to say on multiple sclerosis?

Dr. MASLAND. No, sir.

PERINATAL STUDY

Mr. FOGARTY. Now, you listened to the discussion with Dr. Felix on the progress being made in the field of mental retardation and cerebral palsy. Would you tell us about your work in this field? First tell us about the perinatal study. Has that done as well as you expected?

Dr. MASLAND. Yes, I think this study is progressing very well.

Mr. FOGARTY. Are you including the 40,000 mothers that you hoped for?

Dr. MASLAND. At this time we have enrolled in the study 14,000 women. There have been 9,300 babies born and actually 2,300 of these children have been followed through the first year of life. It is too early for us to have definitive results from the study, since it is quite a job to do a concurrent analysis of the data. We do not have the staff for this.

Mr. FOGARTY. How is the one at Brown University making out?

Dr. MASLAND. They are contributing cases to the study and it is our impression that their data is adequate.

Mr. FOGARTY. Are you satisfied with the progress they are making? Some people complain that they got off to a rather slow start.

Dr. MASLAND. They were very conservative in their start. They felt that until the guidelines had been thoroughly worked out by the committees, it was not desirable for them to begin actual processing of cases, and they held back. At the present time, the cases are well worked up and they are contributing.

Mr. FOGARTY. I thought your goal was to have 40,000 under observation.

Dr. MASLAND. We are reaching the level which will make it possible to reach this.

Mr. FOGARTY. What is that?

Dr. MASLAND. Within this year we will reach a level of new cases that should make it possible for us to reach that level in several years.

Mr. FOGARTY. Is that still 15 institutions?

Dr. MASLAND. That is correct.

There are some very interesting things that are coming out of this. I should emphasize, as I mentioned earlier, that we are not doing a concurrent analysis of the records other than that which is required to be certain that the data that we are getting are accurate and reliable. We can analyze the data later on.

Mr. FOGARTY. What do you mean, later on? Two years from now or 5 or 10 or what?

Dr. MASLAND. It depends on the size of the staff which is doing the analysis.

REQUIREMENTS AND DESCRIPTION OF THE STUDY

Mr. **Fogarty**. You tell us how much you need and we might be able to help you.

Dr. **Masland**. Should I submit that?

Mr. **Fogarty**. Tell us how much staff and what else you need to get this study to the level where it would be the most effective. I think this is one of the most important programs in this field.

Dr. **Masland**. I would be glad to.

Mr. **Fogarty**. And make it a complete report on this program.

(The information requested follows:)

Fiscal Needs for Direct Research Operations for the Perinatal Project in Cerebral Palsy, Mental Retardation, and Other Neurological Diseases of Childhood

Currently (1961) our direct budget for the perinatal project is 111 positions and $1,458,000.

The original President's budget for 1962 provided an increase of 17 positions and $184,000. The revised 1962 budget provides for an additional 23 positions and $146,000, for a total of 151 positions and $1,788,000.

In our professional judgment the total needs for this program in 1962 would be 191 positions and $2,200,000, an increase over the revised 1962 budget of 40 positions and $412,000. Included in the total also are funds to contract for research and production of necessary antigens ($200,000), data processing ($200,000), and contracts for developing and refining necessary protocols and medical examinations ($100,000).

The Collaborative Perinatal Research Project on Cerebral Palsy, Mental Retardation, and Other Neurological and Sensory Disorders of Infancy and Childhood

THE PROBLEM

Neurological and sensory disorders of infancy and childhood constitute a major public health problem in the United States. It is estimated that these disorders afflict 1 in every 16 babies born in this country, or a total of 250,000 babies each year.

Other figures not only emphasize the extent to which these disorders cause long-term disability but also stress the importance of the perinatal period—the period from conception through pregnancy, labor, delivery, and the first month of life. One study has found, for instance that of the childhood disability allowances paid to seriously disabled persons 18 years of age and over under the 1956 amendments to the old-age and survivors insurance program, 94 percent have been paid to persons with neurological disorders and only 6 percent to persons with other disorders. The same study has shown, moreover, that 75 percent of all of these disabled persons suffered their impairment at or before birth.

Of the 4,200,000 children born in the United States each year, 126,000 (3 percent) have some form of mental retardation. About one-third of the estimated 5 million mentally retarded persons in the Nation are children. The annual cost to the States of the 195,000 mentally retarded persons in State institutions is an estimated $250 million. No one knows the cost of supporting those in private institutions or the cost to individual families and communities of the several million retarded persons who are not institutionalized.

There are in this country about 550,000 persons with cerebral palsy. The annual cost of providing special care for 360,000 of these persons is an estimated $216 million.

Because investigators are convinced that conditions during the perinatal period are responsible for a large percentage of all lifelong disabilities, the National Institute of Neurological Diseases and Blindness has organized and developed, in partnership with 15 medical centers throughout the Nation, a research study called the Collaborative Project on Cerebral Palsy, Mental Retardation, and Other Neurological and Sensory Disorders of Infancy and Childhood.

The project just began its third year of operation. It will eventually involve some 50,000 expectant mothers and their children. Data collection begins in early pregnancy and continues through labor and delivery into the early years of the children. Working on the project—at the central office in the Institute, which codes, tabulates, and analyzes the data, and at the 15 cooperating medical centers, where the mothers and children are being studied—are obstetricians, pediatricians, neurologists, and specialists in at least a dozen other medical and related scientific fields. All of them have a common goal: to gain new knowledge about the relationship between events and circumstances of pregnancy, labor and delivery, and the first month of life, and the occurrence of neurological and sensory disorders of infancy and childhood. Their common hope is that this new knowledge will make it possible to prevent these disorders and thereby enable every child to lead a full and useful life.

ACCOMPLISHMENTS OF PAST YEAR

As noted above, the collaborative project is a long-term venture in medical research. It will take several more years to enroll and collect data on all of the 50,000 expectant mothers and their children. This is the minimum number that must be studied, however, if the project is to produce statistically valid results.

This section on the past year's accomplishments of the project, therefore, does not deal with any specific results that could be used as a basis for prevention. It describes, rather, (1) the steps that were taken to improve the machinery of the project, (2) the progress that was made in the processing and the utilization of data already collected by the cooperating institutions, (3) the related studies being conducted at the cooperating institutions to complement the main study, and (4) the early impact of the project on the field of perinatal research and on the teaching of related medical subjects. These developments hold out hope that the collaborative project may soon begin to unlock some of the secrets that today stand between medical science and the prevention of neurological and other crippling disorders of infancy and childhood.

Clarification of objectives

During the past year, efforts were made to define more clearly the objectives of the collaborative project with a view to making more effective use of its machinery. Specifically, the project will investigate the association of prenatal factors with the following abnormal outcomes of pregnancy: (1) fetal deaths (stillbirths), (2) neonatal deaths (deaths in the first month of life), and (3) infant and child deaths. The high autopsy rate (90 percent) of stillbirths and neonatal deaths in the project makes it possible to classify these outcomes in most instances on the basis of (1) specific neuropathological and pathological findings and (2) the detailed description of existing congenital malformations.

The project will also investigate the following abnormal outcomes of pregnancies terminating in live births:

1. Prematurity, by weight as well as gestational age. (It appears that prematurity is particularly important for detailed investigation because of its role as a factor in neonatal deaths as well as in brain damage in childhood.)
2. Congenital malformations of the central nervous system and of other body systems.
3. Manifestations of brain damage. These include:
    (*a*) Severe motor deficits (usually called cerebral palsy).
    (*b*) Mental retardation with or without neurological manifestations.
    (*c*) Sensory disorders, primarily of visual and hearing functions, such as blindness and deafness.
    (*d*) Epilepsy or convulsive disorders with or without other neurological manifestations.

If adequate methods of identification can be developed, such related disorders as speech and language disorders, learning and reading problems, and the so-called organic behavioral syndromes will also be considered for detailed investigation.

The present objectives of the project include the investigation of those factors operating in pregnancy which are known to be, or are suspected of being, related to specific abnormal outcomes of pregnancy. Our knowledge of the role of these known or suspected factors, however, is based on previous studies in which data were collected after the occurrence of an abnormal outcome and hence were subject to bias. A reinvestigation of these factors therefore appears essential.

In addition to confirming or reevaluating the role of such factors, the collaborative project, in which data are collected before the occurrence of an abnormal outcome, will attempt to shed light on the role of related factors, called subvariables. This may further pinpoint pathological mechanisms. Such investigations of subvariables appear feasible because of the rather detailed and complete reporting of the circumstances of each project pregnancy. These include the progress of pregnancy, the existence and the specific nature of obstetrical and nonobstetrical complications, the detailed progress of labor and delivery, and the behavior of the newborn child in the early hours of life.

An attempt will be made in the project not only to study the relation of illness during pregnancy to pregnancy outcome, but also to utilize some measure of severity of a specific illness. Since efforts are now being made to obtain complete information on drugs and medicines taken during pregnancy, it should be possible to determine whether a given disease or its treatment is associated with a given abnormal outcome.

Improvement of research techniques and instruments

The clarification of project objectives made it necessary to consider critically both the procedures for collecting data and the specific items selected for reporting. Also, because the project is a multi-institutional study, it was again necessary to further refine certain aspects of the data collection procedure in order to achieve maximum uniformity in the observation, the recording, and the interpretation of clinical findings at the 15 different medical centers.

For example, the project was being hampered by the lack of uniform criteria for the obstetrical and medical diagnoses which are in general use. Efforts were made, therefore, to design a rather detailed obstetrical summary code which spells out specific criteria for diagnoses, and thus should insure uniformity in assigning diagnoses at the various collaborating institutions. The use of this obstetrical summary code will not eliminate the need for the detailed recording of data. Nor will it preclude the submission of so-called raw data to the central office of the project. It will, however, ease the workload of the central office in coping with the material by furnishing uniform diagnoses which are based on the same criteria. Such information would obviously be of enormous value in that it would enable the central office to make preliminary analyses of project data.

In addition, the experience gained from studying the more than 10,000 cases which have already come under observation has made it possible to make valuable revisions of the methods of examination of mother and child so essential to the success of the project. From the study the participants have already derived important knowledge regarding the reliability and usefulness of the generally accepted methods of history taking and physical examination.

For example, the collection of adequate data on events which have occurred before an expectant mother is enrolled in the project has proven very difficult. These events include her past medical history, her past pregnancy history, and her family medical history. The information obtained from the mother has proven to be incomplete and unreliable. It must be verified. Verification is particularly important with respect to the family medical history; for since the mother is not reporting about herself but about relatives, such a report is second hand. Methods are now being developed which should solve most of the problems of verification.

As to the procedures and forms used for recording data in the postnatal phase of the project (such as those used to test the newborn infant or the 8-month-old child), only minor revisions appeared necessary. With the exception of the revision of the semiannual interval history, they were accomplished.

At present, rather intensive efforts are being made to design a speech and hearing examination for the evaluation of 3-year-old project children, and to develop examinations for the evaluation of 4-year-old children, and for the final evaluation of children at about 6 to 7 years of age.

In order to enhance the availability and utilization of postmortem data on stillbirths and neonatal deaths, a new autopsy record was developed and is presently being considered for adoption as a project research instrument. The use of such a detailed record should facilitate the use of the reported information for research purposes.

To utilize more fully the potential of the detailed investigation that the project will make of the relation of virus infections during pregnancy to pregnancy outcome, more frequent blood sampling of expectant mothers is being carried out. Almost all of the tests for more than 100 different virus infections have been developed. Preliminary testing of blood samples from project mothers for evidence of an earlier virus infection is presently being conducted to gain experience in the testing of large numbers of samples. This activity will be further intensified and will become a regular part of the project sometime during the summer of 1961.

The neuropathology laboratory of the central office received more than 200 brains of stillbirths and neonatal deaths occurring among project cases. These specimens are being studied in a uniform manner.

In addition to procedures for the detailed examination of stillbirths and neonatal deaths, procedures were adopted for the uniform examination of all spontaneous abortions.

Progress is being made in the development of a suitable research technique for the study of maternal attitudes and the emotional characteristics of expectant mothers. Because of the nature of this study and the very large number of mothers involved, it will be necessary to develop a rather limited, brief exploratory device before it can be considered for adoption by the project.

The projected plans for an additional facet of the collaborative project, aiming at the finding of additional cases of cerebral palsy among nonproject children, have gained momentum since a staff member of the central office took on the responsibility of planning for this phase. This aspect of the project will be carefully planned to complement the main phase wherever necessary, but it will probably not become operational in 1961.

Processing and utilization of data

As of the end of 1960, a total of 13,545 expectant mothers had been enrolled in the project, and 8,346 newborns examined. The present rate of enrollment will make possible the addition of about 9,000 new expectant mothers a year.

With an increase in the staff of the central office, it was possible to begin a more detailed exploration of the data already submitted by the collaborating institutions. This activity has resulted in numerous tabulations of various findings reported by the institutions from their observations of project mothers and children. Such tabulations are of the utmost importance. They reflect objectively the extent to which project procedures, including methods of observation and examination, are being carried out uniformly at the collaborating institutions. They also indicate population differences which may not have been taken into consideration in the original design of the project.

To date, these tabulations have also revealed the following incidence rates for some of the pregnancy outcomes which the project is attempting to investigate: (1) spontaneous abortions, about 3 percent; (2) stillbirths, about 2 percent; (3) neonatal deaths, about 2 percent; and (4) prematurity, about 8 to 10 percent.

A preliminary check of all reported data from the examination of 1-year-old project children revealed an incidence rate for cerebral palsy of about 1 percent. This figure is much higher than previously published data have indicated. The number of cases from which this rate was obtained was relatively small, however, and the figure will therefore have to be considered with caution. But if this rate can be further substantiated, the project will yield many more cases of cerebral palsy for detailed investigation than originally expected.

As the staff of the central office increases, it will be possible for the project to realize another important opportunity and responsibility. A study like the collaborative project has both an opportunity and an obligation to utilize already collected data for preliminary analyses of those asociations which appear to occur frequently enough to yield answers, without having to wait until data have been obtained on all of the 50,000 expectant mothers and their children. This is clearly possible for some pregnancy outcomes of a high frequency, such as prematurity.

Such analyses will certainly strengthen the project. They will make it possible to feed back to the collaborating institutions the kind of information which should further stimulate interest. At the same time they will focus attention on areas which show promise for more detailed investigation. And they will also make it possible to identify those areas which appear to show less promise for detailed investigation and hence should not be further explored. Other types of studies are being designed for the solution of these specific problems.

Related studies

To round out the collaborative project, and as a reflection of the increased interest it has generated in the study of neurological abnormalities and other forms of "pregnancy wastage," various related studies have been started at the collaborating institutions. These investigations cover a wide range of areas, such as (1) the detailed assessment of the neurological behavior of newborns and young children by both conventional and highly sophisticated techniques, (2) the neurochemistry of the developing central nervous system in experimental animals in relation to the electrical activity of the brain, (3) the chemistry and pathophysiology of jaundice in newborns, (4) investigations of the problem of the blood-brain barrier, (5) a detailed investigation of maternal-fetal interaction in experimental animals, (6) the relation of endocrinological factors to reproductive failure, and (7) the search for as yet undefined and unrecognized inborn errors of metabolism in children with mental retardation or other central nervous system disorders.

The behavioral sciences also are contributing to this part of the project. This is borne out by specific related studies, such as (1) the evaluation of maternal attitudes and the emotional characteristics of expectant mothers in order to determine whether these factors are related to pregnancy complications and pregnancy outcome, (2) the effect of different child-bearing attitudes and child-rearing practices on the growth and development of children, and (3) the evaluation of the behavior of newborns with a view to determining the relation of certain newborn deviations to future development.

It is apparent that a well-rounded program of related studies has been developed at the cooperating institutions in response to the presence of the collaborative project. As a result many additional important problems in perinatal research are being investigated by interested project personnel at these institutions.

The progress reported above was achieved through the cooperative efforts of the staffs of the central office and the collaborating institutions. This cooperation is reflected in the numerous meetings of project personnel which were held to seek their advice when necessary, to explore the limitations inherent in their respective institutions, and to achieve agreement on alterations and improvements of project procedures and forms as they became necessary. These meetings included workshops to train participating personnel from the various institutions in the use of the data collection methods of the collaborative project.

In addition to this increased contact and communication between the central office and the collaborating institutions, advice was also obtained from numerous consultants knowledgeable in the field of perinatal research, including specialists in the many different disciplines which share an interest in this important field. This contact was not limited to investigators from the United States, but also included European scientists who are well known in their fields.

Impact of the project

It is important to mention here the numerous requests for information, as well as the personal contacts, which were made in the past year by investigators interested in the field of perinatal research to exchange information with the central office, to obtain its advice on the design of their own contemplated studies, and to explore areas of mutual interest. It is obviously very difficult to measure the importance of these activities. It seems reasonable to conclude, however, that the large number of such requests and personal contacts clearly indicates a growing recognition by many scientists of the importance of furthering research in the field of "pregnancy wastage."

Mention needs to be made, too, of the impact of the project on the teaching of such disciplines as obstetrics, pediatrics, neurology, psychology, and pathology at the undergraduate and graduate levels at the collaborating institutions. The importance of accurate recording of observations, as well as the need for more detailed observation in routine patient care, has been recognized. The ultimate effect of this impact in terms of improved patient care, however, cannot be measured at present.

DISORDERS OF NERVOUS SYSTEM OF NEWBORN

Dr. Masland. You might be interested in some of the things which are emerging from this investigation. In the first place, we are being very much surprised, and unpleasantly so, in the unexpectedly high incidence of disorders of the nervous system which this study is revealing. In this series of 2,300 individuals examined at the age of 1 year, 10 percent of them were reported to have some demonstrable abnormality of nervous system function.

Mr. FOGARTY. That is way high; isn't it?

Dr. MASLAND. It was incredible to me. Of course, the 1-year neurological examination is a difficult one. Some of these children may prove to be normal. They may prove to be just a little slow in developing. But these highly qualified examiners rated these children as abnormal.

Now, of this total there were over 3 percent with motor abnormalities. There were 0.7 percent (7 out of 1,000) with visual or hearing defects and these would have to be gross figures to be demonstrable in 1 year.

STANDARDS FOR NORMAL DEVELOPMENT

Dr. SHANNON. One of the big problems this study is running up against is for children in this age bracket. There are no firm physical or developmental standards that have been set in the past and part of the job that Dr. Masland's group has to do is to beat out what are the normal standards for development in these ages, by a series of measurable criterion. This has been one of the real holdbacks.

Mr. FOGARTY. Is this the fourth year we are going into in this study?

Dr. MASLAND. 1962 is the fifth.

Mr. FOGARTY. It seems to me after 4 years we ought to have some standards then. Why don't we?

Dr. MASLAND. We do.

Mr. FOGARTY. What?

Dr. SHANNON. A good part of the past 3 or 4 years has been spent in the evolution of standards. I would hazard a guess a good deal of the records will have to be reviewed on their completion, and I think that the results that Dr. Masland is getting now must be classed in the realm of quite preliminary observations.

Dr. MASLAND. That is true also that this is to some extent a leapfrog type of operation. That is to say we make these examinations at the age of 1 year and we make our best impression on the basis of present knowledge of how to do a good examination. It may take several more years of observation of the children to determine how accurate our present observations, conducted at an early age, really are.

Mr. FOGARTY. Tell us the other things you found to be abnormal.

VARIATIONS AMONG HOSPITALS

Dr. MASLAND. Now, the other thing is the great variation in outcome and in hospital practice which we are observing among these 15 institutions, even though these are very carefully selected strong institutions.

For example, the incidence of reported neurological abnormality varies from 9 percent in one institution to 25 percent in another.

Now, this could be a reflection of variation in criteria, in the methods of examination, but we have done everything we can to see that they are standardized.

Mr. FOGARTY. Off the record.

(Discussion off the record.)

Mr. FOGARTY. Go ahead.

Dr. MASLAND. Now, the next thing is variations in hospitalization.

In one institution 7 percent of the patients are admitted for delivery before they actually go into labor because somebody is worried because there is something out of line in the course of the pregnancy. In another institution this figure is 25 percent. The figures on utilization of forceps for delivery vary from 8 percent in one institution to 59 percent in another.

So it is quite evident that there are tremendous variations in the way things are handled, in the type of problem which different hospitals have, and in the outcome.

And what we propose for this study as it continues is to try to ferret out the meaning and effect of these differences.

Mr. FOGARTY. It is not kept just in that area of cerebral palsy and mental retardation. You may pick up many other things in this kind of examination; is that right?

Dr. MASLAND. That is true; yes.

Mr. FOGARTY. All right. Go ahead.

Dr. MASLAND. From ancillary and related studies, we have some other interesting observations on prenatal factors which relate to outcome. I think it is becoming evident that infection of the baby in the uterus just before birth is a very considerable cause of early neonatal deaths. One of our studies indicates that about 5 percent of the children who died in the first days of life were children who have been infected even before birth.

SMOKING AND PREGNANCY

We have some interesting figures on the role of smoking in relation to pregnancy outcome. In a series of cases studied in Baltimore there was a 64-percent increase in premature births by——

Mr. FOGARTY. What was that again?

Dr. MASLAND. They had two groups of women, women who smoked and women who did not smoke. Among the women who smoked prematurity was 64 percent more common. It was a 64 percent increase, over half again as many of the babies were premature.

Mr. DENTON. 64 percent?

Dr. MASLAND. 64 percent increase. There are some loopholes in this investigation, however. People can always point out that the person who smokes may be a different type of person from the person who does not. Therefore, they say, it is not the smoking that leads to this unfavorable outcome, but it is some other characteristic.

Mr. FOGARTY. Is that what the tobacco people say or is that what the doctors say?

Dr. MASLAND. Some of each.

Mr. FOGARTY. Go ahead, Doctor.

PSYCHOLOGICAL FACTORS AFFECTING CHILDBIRTH

Dr. MASLAND. These investigators also carried out some psychological studies to attempt to pin this down, to see if there were psychological differences and there were. The people who had the premature babies were a more tense type of people and more anxious. But this also seemed to be related to smoking. Apparently both variables—anxiety and smoking—were operative.

There is another very interesting thing that this has led us into: We have been concerned over the question of whether the psychological characteristic of the pregnant woman influences the outcome of her pregnancy. I do not refer to the time-honored old wive's tale of whether she had been frightened by a truck or what not, but simply to the question of a woman being tense and anxious. Several studies now do indicate that the course of labor is more difficult and the pregnancy outcome less likely to be favorable in the case of the tense, anxious type of woman.

Now, in some preliminary studies that we are doing on this question, a number of women were evaluated by questionnaire and other techniques and two interesting things came out of this. Half of these women were not at all sure they wanted to have a baby. It was a rather unexpected finding. Another thing, between two-thirds and three-quarters of them were really frightened at the prospect of their labor.

To me this points to some very important prophylactic measures. Evidently, in our culture, we are not properly preparing women psychologically to have a child.

Mr. FOGARTY. Whose fault is that?

Dr. MASLAND. I suppose it is the fault of our society, and I think that it would be most——

Mr. FOGARTY. I think it might also be, at least partially, the fault of the doctor that is taking care of that person.

Dr. MASLAND. It is more than that. I think the doctor has part of the blame, but I think this goes back throughout the whole lifetime. We are not giving concern to the role of women as being mothers. It is a matter of our school education. It is a matter of the education that the parent gives to the child. We speak of labor pains. We speak of being delivered. The whole terminology of the language relates to this as being a painful——

Dr. SHANNON. Start with the Bible.

Mr. FOGARTY. I was down at the Labor Department today talking to some people at a meeting and this person was telling about his daughter getting married and having her first child and cannot wait until she has her fifth. She wants five or six.

So that is the other side.

Dr. MASLAND. That is right.

MISSION TO RUSSIA

We had this year a mission to Russia which I think has not been mentioned. One of those Russians exchange missions——

Mr. FOGARTY. Were you on it?

Dr. MASLAND. I did not go, but the people who went were individuals from the Children's Bureau and from our consultants who have been particularly interested in perinatal problems. After observing the Russian program, they felt that we are very seriously overlooking the importance of proper orientation of women for pregnancy and labor.

Mr. Fogarty. What did they gain in that trip to Russia?

Dr. Masland. They have a report which should be available within the next few weeks.

Mr. Fogarty. Is it worthwhile? Do you think it is a good report?

Dr. Masland. I think so. I would believe this would be well worthwhile.

Mr. Fogarty. Do you have anything else with regard to mentally retarded or cerebral palsy?

GENETIC CAUSE OF MONGOLISM

Dr. Masland. I think Dr. Felix has touched on the two important direct leads in mental retardation. The study of biochemical abnormalities, and we have several of those new ones and the demonstration of some of the genetic causes which Dr. Shannon alluded to and Dr. Hunt, yesterday. In mongolism, specifically, there is an extra chromosome which is associated with that abnormality.

Mr. Fogarty. What do you mean "genetic"?

Dr. Masland. By genetic I mean related to the gene, which is the protein material in the single cell in the sperm and ovum within which the inherent characteristics of the individual are located.

Now, in mongolism, the abnormality of this genetic material occurs in the ovum shortly prior to the period of conception. The mother usually does not have this abnormality. This is an abnormality that takes place in the ovum just in the last stages of preparation for fertilization and an extra chromosome is located in the ovum. An interesting sidelight of this is in some instances——

Mr. Fogarty. If you know that now what can you do about it?

Dr. Masland. There are two things that are useful here. It has been discovered that in some cases of mongolism, the mother herself actually has this extra chromosome as a carrier. If a woman has one mongoloid child she very often wants to know is there a risk that she will have another. By a tissue culture test it is possible to give her an accurate prediction as to what this likelihood is. Now, the other thing is a lead. We need now to study the processes of ovulation, this final process of preparation of the ovum because something happens in older women that relates to this. The mongoloid child is much more likely to occur in the case of a woman who conceives after the age of 40. It is about almost 10 times as common. It reaches about 2 percent of the women who conceive after 40. This means that something happens in the aging ovary which predisposes to the occurrence of this abnormality of the ovum which it produces.

A number of other forms of mental deficiencies are attributed to abnormalities of this sort.

FINANCIAL NEEDS FOR MENTAL RETARDATION RESEARCH IN 1962

Mr. Fogarty. I think you have given us some real reports of progress in this area but I am not satisfied with it yet. How much more money can you effectively use next year in this field of mental retardation? You may supply that for the record.

(The information requested follows:)

Mental Retardation

The following data, from the National Association for Retarded Children, provides a rough estimate of the incredible financial burden attributable to mental retardation:

"The only figure on which there is broadest agreement (U.S. Public Health Service, National Institute of Neurological Diseases and Blindness, U.S. Children's Bureau, American Psychiatric Association, American Association on Mental Deficiency, National Association for Retarded Children), is the 3 percent figure for the number of mentally retarded in the general population which means 5,400,000.

"The only other figures we know are: (1) that somewhat less than 4 percent of the mentally retarded are either in institutions or committed to institutions but awaiting admission; (2) that in 1958 only 200,000 educable retarded children were in public school classes, and 20,000 additional children in classes for trainable mentally retarded under public auspices.

"The following cost figures are suggested with regard to the 5 million-plus mentally retarded in this country:

(1) Cost of institutional care for 200,000 retarded children and adults in public and private institutions	$300, 000, 000
(2) Annual cost of new institutional construction	100, 000, 000
(3) Cost of special education programs (in excess of the basic public school costs for these individuals)	75, 000, 000
(4) Cost of community facilities for the mentally retarded (clinics, public health nursing, day care, special medical care, counseling and psychiatric care, vocational training, sheltered workshops, and all other community-based programs	75, 000, 000
(5) Cost of special care of the retarded in the family home	500, 000, 000
Total	1, 050, 000, 000

"A State-by-State count probably would show that for 1960 and 1961 item (2) is a low estimate. The same would be true for the education cost estimated in item (3).

"Item (5) is naturally the most difficult to estimate, and our figure of $100 per family is extremely low, but somehow it must be emphasized that a tremendous drain on the general economy of the Nation is caused by the extraordinary expenditures caused the families who have retarded children.

"Taking all these factors into consideration, the annual out-of-pocket cost of mental retardation to the national economy would be a minimum of $1 billion.

"In addition, consideration should be given to a minimum of $1 billion of lost earnings due either to total incapacity (for the small group of severely retarded adults), or to decreased earning potential for the large number of employed moderately and mildly retarded adults.

"The above cost estimates do not include expenditures for research or professional education in mental retardation."

These figures provide an indication of the magnitude of the financial burden. The social burden, measured in terms of unfulfilled expectations, is not so easily delineated, but is probably far more important in its impact upon our society.

In view of the magnitude of these costs, current annual expenditure of the NINDB of approximately $11 million seems small indeed. However, this figure represents an increase during the past year of $2 million. The fact that this program originated only 10 years ago is an indication of the gathering momentum of the research effort. The major emphasis of the program of this Institute is the research directed toward determining the cause and prevention of mental retardation.

The basic ingredient of any research program is the capable and trained investigator. For this reason, the Institute's program has from the beginning placed great emphasis on the importance of training research scientists. Investigators for the future will come from this program. At the present time, the NINDB training program in neurological diseases and blindness is providing training for approximately 950 carefully selected senior scientists. Included are nonmedical investigators trained in laboratory techniques and methods applicable to the study of disorders of the nervous system. It also includes clinicians trained to study diseases as seen in the patient. Of particular interest in relationship to the problem of mental retardation is the newly developing program for the training of pediatric neurologists. This program, which is now providing specialized training for 31 individuals, has as its objective the development of a core of clinical investigators whose particular interest will relate to disorders of the nervous system in infancy and childhood. The number of individuals who have completed such highly selected training is so few at present that it is difficult to establish the necessary training programs to develop the total activity. As new men become available, however, they are including in their research activities responsibilities for the training of additional investigators. Rapid development of this program is anticipated.

There are many causes of mental retardation. Therefore, the types of research projects being supported cover a broad range of medical research. In a large number of cases, mental retardation is evident from the time of birth. For this reason, a major emphasis of the research program is directed toward the study of embryological growth and development, and to the investigation of those factors occurring during pregnancy which may have a harmful effect on the offspring. Laboratory investigations include the study of the chemical changes taking place during embryological development, the transfer of fluids and nutritional substances from the mother to the fetus across the placenta, and the mode of action of toxins and other harmful influences on the fetus during pregnancy.

The recent discovery that certain forms of mental retardation are attributable to abnormalities of body chemistry has intensified the investigation of the chemistry of retarded individuals. In addition to phenylketonuria, now well established as a cause of mental retardation, a number of other similar conditions have been discovered.

New information relating to the cause of Mongolism has now been reported. Many scientists believe it involves a disturbance in the final development of the ovum which takes place prior to conception. A most important related discovery is the fact that Mongolism is many times more common in the children of women over 40 than in children of younger mothers. Further investigation will be needed to determine why aging of the mother should be a predisposing factor in an irregularity of ovum development associated with the occurrence of Mongolism.

At the Laboratory of Perinatal Physiology in Puerto Rico, the Institute has established a monkey colony specifically for the purpose of studying in monkeys the development of cerebral palsy and mental retardation. This colony now comprises over 300 free-ranging animals, and a caged colony of approximately 250. In these laboratories, it has been demonstrated conclusively that cerebral palsy and mental retardation can be produced in monkeys as a result of lack of oxygen at the time of birth. Important investigations have also been conducted on the exchange of oxygen from the mother to the baby throughout pregnancy. Additionally, investigations are being planned to demonstrate the effects of other harmful agents on the developing animal, and to observe the characteristics of the mental retardation which they may produce.

Of primary concern are those factors which relate specifically to humans, and which operate throughout the period of pregnancy, labor, and delivery to influence the health of the offspring. Therefore, a major project of the Institute is its collaborative project for the study of cerebral palsy, mental retardation, and other sensory and neurological defects. The details of pregnancy of approximately 50,000 women are being studied from the time they report for prenatal care until after delivery. The children (approximately 40,000) of these women will be studied at least until the age of 7 years in order to obtain a clear picture of their intellectual capabilities. In those instances where there has been an unfavorable pregnancy outcome, or in cases where a child proves to be mentally retarded, this complete record can be scanned in every detail to determine those factors which may have proved harmful to the child's development. This program, now in the third year of the main phase, is serving to focus attention throughout the Nation on the importance to future generations of providing meticulous care for the pregnant woman, and careful observation of the infant and child.

From these and similar investigations there is already available considerable knowledge regarding factors which can influence the development of the unborn child. Health of the mother is of crucial importance. As mentioned, older mothers are more likely to have an unfavorable outcome. In those instances where the mother has been subject to serious illness, to undernutrition, or to recent miscarriage or other complication, the likelihood of abnormalities is increased. Virus infections, such as German measles, occurring early in pregnancy, may also affect the child. X-ray treatment during pregnancy, or the administration of strong drugs or toxic agents may also influence the fetus. There is even some indication at the present time that excessive smoking during pregnancy may be a predisposing factor in prematurity and impair the child's probability of normal growth.

Maternal and newborn mortality statistics provide an index of the effectiveness of obstetrical and pediatric care. In fact, such mortality statistics can be expected to parallel the frequency of mental retardation. An encouraging progressive decline over the years of the newborn death rate is showing a disturbing leveling off. In fact, neonatal mortality rates over the last 3 years have actually increased. There is cogent evidence that our standards of medical care are not keeping pace with the knowledge available to us. A large share of this responsibility rests with the physician. However, the best medical care in the world will be inadequate if we as a society do not recognize the importance of the childbearing role, and of physical and emotional preparation for motherhood. The Institute's program for the study of causes and prevention of mental retardation will thus fall short of its goal unless it is extended and matched by a program directed toward the study of the ways in which current medical knowledge can be implemented.

Current and estimated NINDB needs for research in mental retardation for fiscal years 1961 and 1962

Program area	Present expenditure, fiscal year 1961	Estimated need, fiscal year 1962
Training	$515,000	$600,000
Research grants	2,645,000	3,600,000
Centers		750,000
Collaborative research:		
Grants	5,100,000	5,600,000
Direct operations	1,458,000	2,200,000
Puerto Rico project	310,000	420,000
Construction		800,000
Intramural	1,096,000	1,150,000
Total	11,124,000	15,120,000

Estimated funds needed for such a program are included in the professional judgment budget presented by NINDB for fiscal year 1962.

SPEECH AND HEARING DISORDERS

Mr. FOGARTY. Tell us about your work on speech and hearing disorders. There is more interest in this problem in the last 3 or 4 years than I have seen.

Dr. MASLAND. That is correct.

Mr. FOGARTY. More people are talking about it, and I am getting many more letters.

HEARING PROBLEMS IN CHILDREN

Dr. MASLAND. We have been conducting surveys of the problem of hearing defects and language disabilities in schoolchildren and in preschoolchildren. It has been demonstrated that if one takes a 30-decibel hearing loss as a criterion—and this is ordinarily considered to be in the range of socially acceptable hearing—there are about 6 percent of the schoolchildren whose hearing is outside of that normal range.

Now this is not necessarily entirely a matter of deafness. One of the important developments is in our ability to distinguish the hearing loss which is attributable to disease in the ear from the hearing loss which is attributable to a disorder of those parts of the brain which are relied upon for the interpretation and evaluation and recognition of sounds and their meaning.

Our program in medical audiology is concerned in training people to investigate this rather neglected field. But by a certain new technique, electroencephalogram and other procedures we are learning to distinguish true deafness—actual ear difficulties—from inability to recognize sound due to disorder of the brain. The importance is that the training procedure which is required is quite different. In the case of the individual whose ear is damaged, you are almost forced to use a procedure which does not make any utilization of sounds. In the case of the individual who is not able to interpret and recognize sounds, a training procedure which teaches the child to concentrate on sound and brings it to his attention, may eventually make it possible for him to develop useful hearing and, equally important, understandable speech.

OTOSCLEROSIS

Now in the adult group, our important advances are in the treatment of otosclerosis.

Mr. Fogarty. What is that?

Dr. Masland. Otosclerosis is a condition of adults in which the small bones which transmit the sounds from the eardrum to the ear become hardened and stiffened so that they can no longer vibrate. There have been progressive advances in the technique for alleviating this condition using little pieces of plastic in place of the stiffened bones, or using little pieces of vein tissue from other parts of the body to replace these thickened structures with a thin structure capable of vibrating. The results of this are incredibly dramatic. You have a person who has been deaf for years. He is isolated from the environment, cut off as a deaf person is, with a change in quality of voice and all the other characteristics that you look for with deafness. Overnight, with this operation, the voice starts to change back, they become a member of the community and they are normal people. This operation is about 80 percent effective in selected individuals.

REQUIREMENTS FOR MORE INTENSIVE WORK WITH HEARING AND SPEECH DISORDERS

Mr. Fogarty. All right, so you have this information. What are you doing with it?

Dr. Masland. One of our big concerns here is in the training of highly skilled investigators in this area. This is another neglected field, and our training program is just really starting.

Mr. Fogarty. You are not going to increase it much with your budget?

Dr. Masland. We have a strong program at this time, and we will be able to maintain it at its present level.

Mr. Fogarty. That is not anything to brag about, is it? You could use a lot more money in training in this area, I think.

But now that you have this information, what is the quickest way we can get it to the people who need it—through the school systems or through the medical societies or what?

Dr. MASLAND. I think through both.

I think actually the dissemination to the medical societies is pretty prompt through the meetings of the organizations.

Mr. FOGARTY. That does not get it to all children, though?

Dr. SHANNON. Mr. Fogarty, I think one of the most effective techniques here to carry this type of observation to the people is by broadening the community health service program, comparable to what is planned for the new Bureau of Community Health. Because we are here dealing on a local level, with different forces operative in bringing services to the people, depending upon the local situation. In some cases it will be via the schools, and in other cases via the Department of Health and the like. I think the primary value of our technical assistance program is in the Public Health Service, that they can get at the problem at a local level.

Because any service of local levels will have such a diversity of operation that in the absence of that contact, it is very difficult to apply information.

Mr. FOGARTY. Well, I think this is a good example of the lack of application of medical knowledge at the local level, isn't it?

Dr. SHANNON. Well, this is so recent I would not feel badly.

Mr. FOGARTY. Do you make any recommendations as to what the Office of Education ought to do in this field?

Dr. MASLAND. I could prepare a report on that.

Mr. FOGARTY. You have not had any dealings with the Office on the top level here?

Dr. MASLAND. No, sir. I have with the Community Health Group.

Mr. FOGARTY. I would think that would be an area where we should be working together.

Dr. SHANNON. Also rehabilitation.

Mr. FOGARTY. Yes. I wish you would get me some suggestions and place them in the record.

Dr. MASLAND. Yes, sir.

(The information requested follows:)

SUMMARY OF HEW PROGRAM IN SPEECH AND HEARING

Training of investigators

There are no investigators being specifically trained for case finding or case-finding techniques. But this activity is included in the other training programs.

The NINDB is supporting the training of highly skilled professionals in the methods of diagnosis and treatment of speech and hearing disorders. There are 27 programs in otolaryngology (150 trainees). There are 4 programs for the training of investigators in medical audiology, and there are 24 research fellowships in this area. These programs involve both children and adults.

The Office of Vocational Rehabilitation is providing research training at the predoctoral and postdoctoral levels, having at present 15 awards. These programs are concerned with training for research in methods of management and rehabilitation of adults. The Children's Bureau is supporting training grants and fellowships in audiology and speech pathology and has five such training grants.

There are no programs listed to develop investigators for the study of management, training, and education of children. It must be recognized that the problems of the child with speech and hearing disorders are entirely different from that of the adult in need of rehabilitation.

Support of research

The Division of Chronic Diseases is particularly interested in the development of case-finding techniques through which the hard-of-hearing individual may be detected. The Office of Education is also concerned with the development of effective screening techniques of children of school age and for the detection of disability at an early age in the preschool child.

The NINDB Biometrics Branch is assembling data on incidence and prevalence, and this Institute is also supporting a broad project of the American Academy of Ophthalmology & Otolaryngology for determining the effectiveness of audiometric screening in the recognition of hearingdefects; to establish norms for hearing of schoolchildren; and to determine the incidence and significance of hearing loss at this age. The Children's Bureau is also contributing to this program through their affiliated demonstration project.

The NINDB is supporting a number of projects concerned with the diagnosis and treatment of disorders of speech and hearing—supporting at present 106 such projects in the amount $2,210,000 for 1961.

The Office of Vocational Rehabilitation is supporting 46 research and demonstration projects primarily concerned with the evaluation of training and rehabilitation techniques for the adult.

For children, the Children's Bureau is supporting five demonstration projects in speech and hearing and six in relation to cleft palate. Support is through funds and technical assistance. These demonstration projects relate to a variety of functions including case findings, the techniques of administration of medical, surgical, and audiological care, and to some extent the utilization of training procedures. It does provide some research in each of the three areas of case finding, therapy, and management.

The Office of Education within its "cooperative program" is supporting 20 projects on the effects of various conditions as a deterrent to speech and language development, and 7 other projects having to do with communication problems of the mentally retarded.

Dissemination of information

The dissemination of information is conducted primarily through publications and conferences. Each of the several agencies has utilized these means. NINDB supports approximately two conferences a year for exchange of scientific knowledge and review of the field. The OVR has utilized conferences as a method of program planning, as has the Children's Bureau. The Office of Education has also utilized conferences and publications for the establishment of professional standards and as a means of upgrading practices throughout the country. The regional offices of OVR and the Children's Bureau are important factors in this process.

Training personnel to provide services

The Office of Vocational Rehabilitation has 30 training programs in speech pathology and audiology. The purpose of these programs is to train personnel for the diagnosis and management of speech and hearing problems in the adult. None of the PHS programs are for medical education. There are no programs in the Federal Government specifically to support the training of therapists or educators for children with speech and hearing defects.

Providing services

The grants-in-aid program of the Children's Bureau provides basic support for speech and hearing services in most of the States. No other Federal support services (except as demonstration projects) is noted.

The following table summarizes the overall program.

Department of Health, Education, and Welfare

	Adults			Children		
	Case finding	Diagnosis and therapy	Management	Case finding	Diagnosis and therapy	Management
1. Training of investigators for	----------	NINDB	OVR	----------	NINDB	----------
2. Supporting research in	DCD OVR	NINDB	OVR	OOE NINDB	NINDB OOE	CB OOE
3. Disseminating information about	----------	NINDB	OVR	OOE	NINDB	OOE
4. Training personnel to provide services	----------	OVR	OVR	----------	----------	----------
5. Supporting services for	----------	----------	----------	----------	CB	CB

Key:
DCD—Division of Chronic Diseases, Public Health Service.
NINDB—National Institute of Neurological Diseases and Blindness, Public Health Service.
OVR—Office of Vocational Rehabilitation.
OOE—Office of Education.
CB—Children's Bureau, Social Security Administration.

UTILIZATION OF NEW KNOWLEDGE IN AUDIOLOGY AND SPEECH PATHOLOGY

This proposal is forwarded in response to the request of the chairman of the House Appropriations Subcommittee on HEW for recommendations as to what we ought to do in the Department of Health, Education, and Welfare, and especially in the Office of Education, in the field of speech and hearing disorders. Before presenting such recommendations, it was considered desirable to review the activities of each of the several agencies having an interest in this broad field. The following report does not necessarily represent the views of the several agencies. It represents only the professional views of the Director, NINDB, in response to the subcommittee chairman's specific question.

A truly effective total program for medical services requires (1) an adequate program for case finding, (2) effective procedures for the diagnosis and medical therapy of afflicted individuals, and (3) practical programs of management involving retraining educational techniques and social rehabilitation. For each of these parts of the program, there are certain necessary steps in program development as follows:

1. Training investigators. Continued advances in a field depend upon the availability of highly trained and competent research personnel.
2. Conducting and supporting research.
3. Disseminating throughout the profession the newer knowledge developed from research.
4. Training therapists and teachers in utilizing the new knowledge.
5. Establishing clinical services to bring this knowledge to the handicapped individual.

A study of the preceding "Summary of HEW program in speech and hearing" reveals certain gaps in our total program. There has not been any program focused on the training of individuals to conduct research in educational methods, and probably for this reason there has been a relatively small research program in this area. It is probable also that knowledge which has been derived from research in the classification of language disabilities has not been disseminated widely throughout the profession and made available to those individuals atempting to develop educational methods.

An important advance of new investigations in the field of speech and hearing is in the ability to demonstrate and differentiate the various specific defects of hearing and of brain function which manifest themselves as failure to develop normal language. A parallel need now is to discover educational techniques which will reflect this newer knowledge, providing for each child a form of training appropriate to his handicap. Until this is accomplished, large-scale training of therapists is of questionable value. The trainees will contribute little to the patient unless there is available an adequate diagnostic program and unless the therapist can be trained to take full advantage of the findings of accurate and complete diagnosis.

The problem is complicated because the several disciplines involved in studying speech and hearing have, in general, different emphases in their interests. Medically based programs have concentrated on the study of etiology and differential diagnosis. Centers for speech and hearing in the universities have placed their emphasis on language mechanisms, and have also carried the major responsibility for developing techniques of individual patient instruction. The field of education within which 90 percent of the language handicapped children must be taught, has concentrated on training teachers for classroom type instruction. This field has contributed less in developing techniques and in training teachers for individual types of instruction for the child with hearing and/or language disability.

The following measures are recommended for correcting the several defects of our total program noted above:

1. The "demonstration" project has proved an effective means for evaluating practical methods for diagnosis and treatment as well as for management, training, and education. It can be made a useful instrument for disseminating knowledge at the professional level. The program in the field of speech and hearing could be strengthened through the development of additional demonstration projects. The continued development of those programs which have been instituted for adults by the Office of Vocational Rehabilitation and for children by the Children's Bureau would be most desirable.
2. With these strengthened demonstration projects as a base, the opportunity for continued development of the parallel programs of research training and research fellowships will exist. These centers can thus provide a locus within which there can be trained skilled investigators in the medical and diagnostic problems of speech and hearing as supported by NINDB, and in management techniques as supported by OVR.
3. The demonstration projects should also be utilized more widely for orienting the profession, especially those individuals now responsible for the training of teachers and therapists throughout the country. Workshops, seminars, and conferences through which such individuals will become acquainted with the programs and techniques developed in the demonstration projects are an important means through which this could be accomplished.
4. The above still does not provide a means for increasing the involvement of the educators in this total program and for encouraging the development of a broadly based research program in educational techniques. Certainly it is from the educator that one must expect to develop the most advanced research on the educational methods to be used for the management of language disabilities.

Opinions differ as to the proper role of the field of education in this total program. One opinion is, "The problem is primarily one of education. The vast majority of these children with speech and hearing disabilities must be dealt with and taught within the school system. If we place upon the educators the responsibility for training an adequate number of teachers for this job, they must inevitably become involved in all aspects of the program, and there will develop within the field of education centers not only for teacher training, but also for the sorely needed research in educational methodology in this field."

Another opinion is quite different: "The whole orientation in the field of education is toward classroom type of group instruction. Our problem, however, is one of individual type training. We are not dealing with teaching but with therapy. To ask the educators to enter this field would require them to undergo a fundamental reorientation of their approach. It is more logical to develop a specialized field of speech and hearing within the orbit of the university and the medical school, and to rely on this group to provide the trained therapists to work within the school system (just as nurses and doctors provide services within this sytem)."

My opinion is that there is truth in both these positions. In the past, the major contribution to speech and hearing has probably come from specialized departments outside the regular educational circles. For the time being, we must continue to rely heavily on these sources. However, the magnitude and the very nature of this problem demand that eventually it be dealt with as an integral, if specialized, aspect of the total educational program. If the field of education is not now oriented toward such specialized instruction, then it is high time that a fundamental reorientation take place. There are evidences that this reorientation is in active process in related fields such as that of mental retardation.

At present it probably would not be desirable to launch a large-scale Federal program for training language therapists. It would be preferable to concentrate on developing centers within the field of education to study educational techniques in language handicaps. Within these centers programs also could be developed to train the highly skilled investigators required to conduct this type of research. In addition, a research fellowship program could become the basis for the future healthy development of a scientifically based research and training program in speech and hearing within the field of education. In this program, carefully selected educators would receive research training which could include a period of exposure to the diagnostic and therapeutic programs of the demonstration projects. Equally deirable would be fellowhips which would permit individuals in advanced training in the medically centered programs to have an opportunity for advanced study in the institutions of education so that two-way exchange of information could thus be encouraged.

The emphasis of the Federal program in the field of education would thus parallel that in other areas—the emphasis would be on research and on the training of invetigators, using this as a method for raising the standards for the training of practitioners, a vast responsibility which at the present time rests primarily upon the States.

It is believed that these several recommended procedures could have a major influence in forwarding research and development in this field, and in promoting the rapid utilization of new knowledge in improved patient services.

PARKINSON'S DISEASE

Mr. Fogarty. Now on Parkinson's disease. Do you think you have some hope here?

Dr. Masland. Yes; there are several approaches to Parkinsonism.

Mr. Fogarty. The operation that some doctors were performing a few years ago turned out not to be too successful; is that right?

Dr. Masland. It is certain that an operation is not a complete answer for Parkinsonism. But on the other hand, the refinements of this technique carried out by Dr. Cooper and by others show that for the relief of symptoms, at least temporarily, it does have a place. It produces a temporary relief of symptoms. And I do not think these patients have been followed long enough to know how permanent it may be.

We also have drug treatment for Parkinsonism which again is only a matter of relieving symptoms. What we must do is get at the cause. I have previously mentioned that some of these cases are due to an infection. The other important lead relates to the fact that this may be a chemical disturbance, or a disturbance in the aging process of the cells. Parkinsonism is, in general, a disease of older people.

Dr. Felix referred to the fact that certain of the tranquilizing agents produced Parkinsonism, and this is an incidental observation and an annoyance to the psychiatrist. But to the neurologist this is an observation of extreme moment: What is the chemical affinity of this tranquilizing drug, where does it have its effect, how is it that this can mimic a condition which appears spontaneously in other people?

There is another interesting clue that manganese poisoning, which used to be rather common in this country, and still occurs in certain foreign countries, produces Parkinsonism. It is a terribly dramatic thing, the terrific rigidity and incapacity that occurs in people poisoned with manganese, which you get from manganese dioxide dust. Interestingly enough, there are chemical relationships between the enzyme systems, the chemical systems in the brain, which have an affinity for manganese and for certain of the tranquilizers. And we need a strong chemical attack on those diseases.

Mr. FOGARTY. Well, if you need a strong chemical attack, you need some more money for it.

Dr. MASLAND. Yes, sir.

Mr. FOGARTY. You are not going to do it with your budget.

EPILEPSY

Now epilepsy. You also said you could see some progress in epilepsy. Is it true about 80 percent of all epileptics can be treated or controlled with known drugs?

Dr. MASLAND. That is correct, that approximately 80 percent of epileptics can have at least partial control of their seizure with drugs. It depends on the population with which you are working whether you can obtain complete control in that high proportion.

Mr. FOGARTY. Dr. Bailey told us 3 or 4 years ago about this young fellow, referred from the University of Virginia Medical School who had this operation. Have you followed up this case?

Dr. MASLAND. I do not know the outcome of that. We followed a series of 88 operated cases. Of these, 38 percent were seizure free, while 75 percent were considerably improved.

(A more detailed report on epilepsy follows:)

EPILEPSY

THE PROBLEM

With an estimated 1,700,000 epileptic persons in the United States today, the economic and social burden has been extremely heavy. New medical and surgical treatment now available makes it possible for more than half of these persons to have their seizures controlled. Most of these persons are capable of regular productive employment but various laws and outdated thought covering the disorder make employment opportunities difficult to find. Fortunately, steps are now being taken to insure the employment of epileptics who have been rehabilitated through advances of science.

Encouraging reports come from a number of medical research centers and hospitals. One prominent U.S. institution reports that in their series of epileptics, 19 percent have made superior adjustments, 68 percent are self-supporting, 9 percent are partially dependent, and only 4 percent are totally dependent. Moreover, adjustment was not altered by type, frequency or duration of seizures.

NEUROLOGICAL RESEARCH ACTIVITIES

At the present time, most epileptic patients are treated through drug therapy. A small percentage, however, have been found to benefit significantly from surgical treatment. These are patients in which the seizures arise from a single focus in the brain. Among these, those whose focus lies in the temporal lobe have been particularly amenable to surgery. Surgical research for this type of epilepsy at the National Institute of Neurological Diseases and Blindness has freed a large percentage of cases from seizures and has drastically reduced the number and severity of seizures in others.

The basic research at the Institute in functioning of the brain, and particularly the research in biochemistry of the brain, is advancing more accurate knowledge concerning the role of certain normally occurring chemicals in the brain which are capable of influencing electrical discharges which, in turn, influence susceptibility to seizures.

The most important immediate concern is to determine the nature of the abnormal activity of the brain which leads to the occurrence of the epileptic seizure. There is now strong evidence that local or general abnormalities of body or brain chemistry may lead to overexcitability of the nerve cells and a predisposition to seizures.

This year one investigator studied the reactivity of patients with epilepsy to a variety of injected convulsant drugs—caffeine, metrazol, strychnine, acetylcholine, and fluorofatty acids. The reactions to these drugs were different in different patients—some individuals showing hypersensitivity to one of these drugs—others to another. The investigator concluded that these differences in sensitivity reflected basic differences in the chemical aberrations underlying the disorder. A clue regarding the nature of these aberrations stems from the discovery that gamma-aminobutyric acid (GABA), a naturally occurring amino acid of the brain, has an important role in regulating nervous excitability. Defects in the enzyme systems concerned with the synthesis of GABA are known to cause seizures. The Institute is supporting a number of projects directed toward the study of these enzyme systems, and has an important intramural program in this area.

It is known that physical injury of the brain may produce a scar, and result in recurrent epileptic seizures. The mechanism through which this scar creates an irritable focus is unknown. Studies of the electrical activity of the brain and its individual nerve cells under normal and abnormal conditions are elucidating this mechanism.

Paralleling this research are investigations of the modification of excitability of the central nervous system through the use of anticonvulsant drugs. As research in epilepsy has advanced during the last decade, many new drugs for the treatment of this disorder have become available. At one time, a physician decided between bromides and phenobarbital. Today, the treatment prescribed depends upon a number of factors: The type of disorder, the age of the patient, and many other considerations. A large percentage of epileptic patients are now able to effectively maintain control of seizures through various anticonvulsant drugs, used singly or in different combinations. Proper control of seizures in this group may be obtained through working with the physician to determine the most effective treatment possible.

Unfortunately, there has been no corresponding carefully planned evaluation of the results of the use of these drugs. The development of new and more effective agents, and the prompt and critical evaluation of their effectiveness is now an important part of the Institute's program.

PROSPECTS FOR THE FUTURE

This year the Institute sponsored a symposium on the evaluation of drug therapy for the treatment of neurological and sensory disorders. Eight panels of well-known scientists considered the problem in relation to particular disorders, including epilepsy.

The panel has worked out a method of classification of cases and a preliminary form for use in a statistical analysis of results. The various drugs must be evaluated over a period of time with many patients to determine their effectiveness, toxicity, and total bodily effects in relation to each of the many types of epilepsy.

Seizure actively can be influenced by many factors in addition to the chemical ones discussed in this report. Two major contributing sources are perinatal injuries to the brain and accidental head injuries. The ultimate solution of these problems will depend upon the ability to recognize and define in each individual the nature of the defeat, and to correct it with the treatment most capable of restoring a normal situation.

Although improved control with medicine has decreased the enrollment in special schools for epileptics—in one school by two-thirds—the fundamental need is prevention and cure. Until a preventive and cure are found for epilepsy, research on medical and surgical care offers considerable value in lessening the national burden from this group of ailments.

MIGRAINE HEADACHES

Mr. Fogarty. We have heard a lot about migraine headaches over the years. Has anything been developed that will relieve severe migraine headaches?

Dr. Masland. Several drugs are available, and there is a new one this year, still only in its preliminary evaluation, which offers some hope of relief.

INTERNATIONAL RESEARCH

Mr. **Fogarty.** Now, international research. You spoke about that in your opening statement and indicated that you would like to expand this. It works both ways, doesn't it? We help these countries with our know-how and the information we have, and they help us.

Dr. **Masland.** That is correct. I think that this type of a bilateral activity, where you have maximum exchange of personnel and the joining together for a common interest, is one of the strongest ways of strengthening both teams—both members of the team.

Mr. **Fogarty.** What is the organization that Dr. Bailey heads? I met him in India, and he was visiting several countries in that area.

Dr. **Masland.** The World Federation of Neurology.

Mr. **Fogarty.** World Federation of Neurology. I was very pleased with the acceptance he is getting in all of these countries. He says that interest is high and that the local governments are putting up the money to cooperate with this world federation.

Dr. **Masland.** That is right.

Mr. **Fogarty.** I assume that you work with them?

Dr. **Masland.** We work with them very closely. The World Federation of Neurology has a number of "problem commissions," groups of scientists, each with a given area of concern or interest, and each of these commissions is maintaining an overview of the status of the field and, as a group, is developing programs. The Commission on Epidemiology and some members of our staff are participating in that. This group is planning studies on a worldwide basis, to answer specific problems about the distribution of disease, such as ones which I spoke of, multiple sclerosis, for example.

Our observation has been that, particularly in the newly emerging countries, the thing those people are most anxious for is a contact with scientists in this country for exchange of information and experience.

Mr. **Fogarty.** He said there is a big meeting in South America this coming fall?

Dr. **Masland.** Yes.

Mr. **Fogarty.** Do you expect to attend?

Dr. **Masland.** I have not made definite plans one way or the other.

Mr. **Fogarty.** When I left him he was going to visit three or four countries and was coming back through this country.

Dr. **Masland.** He is here now.

Mr. **Fogarty.** He is here now? Well, you would not be embarrassed if I asked him what he thought of this appropriation, would you?

Dr. **Masland.** No, sir. I do not think he would embarrass us.

Mr. **Fogarty.** He was never very backward when I asked him what he needed. He always told us without much delay. I think that is one of the reasons you have a good Institute today.

Dr. **Masland.** I believe so.

Mr. **Fogarty.** Mr. Denton.

MULTIPLE SCLEROSIS

Mr. **Denton.** I want to ask just a very few questions. Is multiple sclerosis prevalent in Australia?

Dr. MASLAND. In certain parts of Australia. In the colder parts of Australia, yes.

Mr. DENTON. I know a young lady whose husband is a naval officer, and she came to this country and apparently had multiple sclerosis. Now does the fact that she came from Australia to this country have anything to do with it?

Dr. MASLAND. Well, it could have.

Mr. DENTON. Yes.

Of course she is the wife of a naval officer, and they have lived all over the world. Apparently it gets better and then it gets worse.

Dr. MASLAND. In multiple sclerosis, the disease occurs in episodes.

Mr. DENTON. In what?

Dr. MASLAND. In episodes. A person will be perfectly well, and then rather suddenly there will be an attack of weakness, paralysis, dizzyness, numbness, some affliction of the nervous system. And this is due to the liquefaction of the nerve sheath which you spoke of. Now this may pass off and the individual will have at least some recovery of function. It may go for 6 months, for a year, for a lifetime without another attack. But in the majority of instances sooner or later another episode occurs. Maybe it hits in the same place, maybe it hits somewhere else. The person gets a little worse. Then this repairs, and the same process occurs over and over.

Mr. DENTON. This young lady I know of could not see out of one eye. She went out to the naval hospital and that went away, but then she seemed to have trouble walking.

Dr. MASLAND. Yes. This is quite a characteristic story.

Mr. DENTON. Now that has gone away. But the naval hospital said it was multiple sclerosis.

That is all.

MYASTHENIA GRAVIS

Mr. FOGARTY. Doctor, I did not ask about myasthenia gravis. What is happening in that field?

Dr. MASLAND. There are two leads in myasthenia gravis. We have drugs which alleviate symptoms, prostigmine and other related drugs. Investigators at Bethesda have been working with a new similar drug which seems to have some promise of improving our ability to alleviate symptoms. This is not curative.

Mr. FOGARTY. What is that drug?

Dr. MASLAND. This is galanthamine.

Mr. FOGARTY. Is that the drug from daffodils?

Dr. MASLAND. Yes.

Mr. FOGARTY. I think maybe if you had asked for money a year ago to do some research on daffodils, we might have gotten laughed right off the floor of the House when we presented the bill. But that new drug from daffodils shows promise in the treatment of myasthenia gravis?

Dr. MASLAND. Yes. There is another thing in myasthenia, that is, some suggestion that this may also be an autosensitization, an allergic phenomenon which I mentioned earlier in multiple sclerosis. In this instance, the offending tissue is in the muscle. It is thought to be the sensitive protein of the muscle which is the "trigger" mechanism for causing the muscle to contract. When the nerve impulse reaches the end of the nerve where it joins the muscle, it liberates a certain chemical, and that chemical reacts with the muscle instantaneously and triggers off a contraction. The suspicion is that this sensitive protein of the muscle is damaged by immune substances in the blood, and this makes it incapable of responding to this chemical in the normal fashion.

Mr. FOGARTY. This is a cousin of, or similar to, multiple sclerosis, isn't it?

Dr. MASLAND. That would be a similar type of reaction. The disease is quite different in its manifestations. It is a weakness, a generalized weakness of the body.

RETROLENTAL FIBROPLASIA

Mr. FOGARTY. I have one final question on retrolental fibroplasia. One of the issues of Public Health Reports showed a survey of five States. It does not say where. It shows how new cases have gone down from 278 in 1950 to 3 in 1958. Is there anyway you can get a similar table, countrywide, and supply it for the record?

Dr. MASLAND. I will see what I can find.

Mr. FOGARTY. There is no reason why this should occur any more, is there?

Dr. MASLAND. A few cases occur in premature babies even though they have not received oxygen, but very few, as you see in this table. There were only seven in 1958, and there are probably fewer now. They are still working on the mechanism through which this blinding disorder occurs in those few cases.

Mr. FOGARTY. Will you see if you can get a nationwide table similar to this and put it in the record?

(NOTE.—Dr. Masland subsequently indicated that the national data requested is not available.)

Do you have anything else you would like to say?

INSTRUMENT DEVELOPMENT

Dr. MASLAND. There was one other thing which I thought I might mention.

I spoke earlier in regard to the role of instrumentation. of the development of new instruments as tools for the neurologist. There are several areas here——

Mr. FOGARTY. What do you mean by tools?

Dr. MASLAND. Instruments. Well, here is an example——

Mr. FOGARTY. You mean instruments that a neurologist would use in working on human beings, or in research, or what?

Dr. MASLAND. I am speaking here, for example, of a computer as an instrument. Now here is an instance where we wished to be able to record the response of the brain when a light is flashed into the eye. This is one way of testing vision in infants, it is a way of testing vision under rigidly controlled circumstances where you do not have to rely on the subject. Now the problem here is that when you record the electroencephalogram through the skull, there is so much background irregularity of the record that the response of the brain to the light flash does not show up. The question is, How can you devise a method whereby that little response will show up? And you do this by adding responses. You throw in a repeated stimulus, and you add the responses of each. The random irregularities cancel out, but the consistent response to your stimulus adds up, and eventually shows on the record.

I have a record to show you what this looks like. The top wiggly line is the response to a single flash of light, and you cannot see it because there is so much irregularity.

Mr. Fogarty. I can see the line all right.

Dr. Masland. You can see the line, but you cannot see any response. If you take a number of those and superimpose them, you get this wide line below it. That is also just as unreadable. But using this instrument you add the responses and cancel out the irregularity, and you end up with the curve such as this at the bottom. This is the summed response of 1,500 light flashes.

Mr. Denton. What does that mean?

Dr. Masland. This means a light was flashed in this person's eyes 1,500 times, and each time the response was run through a machine and added to the previous response. And then the sum total is traced off on this line. So the result of this is to bring to light a response of the brain that otherwise would be completely lost, making it apparent.

Mr. Fogarty. All right. Now what is your problem?

Dr. Masland. Now this is merely an example of the type of instrumentation which provides the investigator the ability to observe responses that he might otherwise completely overlook. But this sort of instrument can hardly be developed by the medical scientist. It requires a cooperative team arrangement, usually with industrial scientists who have the know-how.

Mr. Fogarty. What is your problem?

Dr. Masland. Well, the problem is that this type of investigation is expensive.

Mr. Fogarty. How much do you need? Well, why don't you take your time and supply a statement for the record on this—what is needed and why we ought to do something about it?

Dr. Masland. Yes, sir.

(The requested report follows:)

Instrument Development

The extent to which advances in medical knowledge have stemmed from advances in instruments and techniques available to the scientist is not generally recognized. The scientist has always been dependent upon instruments for his investigations. However, within the last few years technological developments have been so rapid that methods available to the scientist have multiplied almost beyond his ability to utilize them. Additional creative technologists must be enlisted to work with scientists, both in the development and in the application of instrumentation to medical research.

A review of past advances serves to emphasize the importance of instrumentation in a variety of medical research techniques.

The discovery of the microscope and its development in the 18th and 19th centuries made possible the demonstration of the existence of microorganisms. It thus provided scientific validation for investigators proposing a germ cause of disease.

Similarly, the microscope has made possible over the years our present detailed knowledge of the minute structure of the human body and the mechanisms through which the organs are active.

Within the past 20 years the usefulness of this instrument has been broadened through the discovery of the electron microscope—a new instrument capable of magnifications almost to the order of 1 million times. This instrument is now so sensitive that it can magnify with clarity structures little larger in size than a hydrogen atom. It is providing us tremendous new knowledge regarding the physical and chemical reactions of the body structures, and their modification in health and disease. Even the smallest virus particles are visible under this amazing instrument, and the penetration of these infectious agents into the tissues of the infected animal can be studied visibly.

Without these progressively refined instruments our present knowledge of the human organism would be severely limited. Each new refinement opens up a whole new vista of medical knowledge.

The discovery of the vacuum tube has made possible incredible advances in the effectiveness of human communication over long distances. Less well recognized is the contribution which this invention has made to our knowledge of communication within the human nervous system itself. The nerve impulses are associated with electrical changes capable of measurement by sensitive instruments involving the vacuum tube and other systems of electrical amplification.

Our present knowledge of the activity of the nervous system has stemmed largely through the availability of refined amplifying instruments. A practical example of the application of such techniques is the electroencephalograph. This instrument is simply an extremely sensitive electronic amplifier capable of recording the minute fluctuations in electrical field which take place in the normal and diseased brain. The fluctuating electrical "brain waves" are of such magnitude that they can be recorded with this sensitive instrument through the scalp of a patient without causing the patient discomfort.

This instrument is finding daily use in numerous clinics throughout the world in the diagnosis of epilepsy, brain tumor, and other disorders of the brain. In addition to its usefulness in diagnosis, it has advanced markedly our knowledge of the function of the nervous system and the distortions of neural activity which take place in disease.

Further refinements of these recording techniques are now making it possible in animals to observe the activity of the smallest unit of the nervous system—the cell. The detailed study of the cell—alone and in aggregates—is fundamental to a further understanding of the action of nerves.

In recent years it has been discovered that certain forms of mental illness, and of other conditions involving the occurrence of involuntary movement and tremor, may be relieved, at least temporarily, through selective destruction of abnormally overactive portions of the brain. The areas to be inactivated are often deep seated and may be reached only by surgical intervention. Surgical techniques for such inactivation have been quite successful, although the passage of instruments into the brain has been necessitated.

Recently it has been discovered that high frequency sound waves accurately focused on that portion of the brain to be inactivated may produce a local effect without involving damage to intervening tissues. Further refinement of this technique may provide a most useful tool for selective inactivation or destruction of abnormally functioning areas of the nervous system.

One need not mention the fundamental value of X-ray in the diagnosis of human disease.

Less well recognized is the increasing usefulness of radioactive elements for the study and treatment of disease. Among the new techniques for use of radioactive elements is the "brain scanner." This instrument is capable of detecting the presence within the brain of minute traces of radioactive elements which are concentrated in diseased areas, particularly tumors.

Advances in chemical techniques are less spectacular, but their contribution to medical knowledge is no less impressive. Chromatographic analysis of complex chemical mixtures is ideally suited for the study of body fluids and permits the rapid search for abnormal constituents in a large number of patients over a short period of time.

Similarly, electrophoresis for the separation of proteins, and the recording spectrophotometer for the analyses of chemical compounds, increase the effectiveness of the laboratory scientist by many thousandfold. Through the use of these techniques a small number of highly trained scientists can carry forward the work which previously would have required a lifetime of research by many investigators.

There are, however, unmet needs. It is believed that the techniques required to meet these needs are available and should be marshaled for their solution.

Specifically, there is need for an instrument capable of carrying forward an automatic analysis of the cellular structure of tissue sections of the brain.

Within each animal brain are literally billions of neurons. They are assembled in clusters or aggregates called nuclei, and each nucleus subserves a specific function having to do with sensation, intellect, or movement.

It is believed that the distribution of neurons within these nuclei relates very closely to the performance of the individual in health and diseases. It is almost a certainty that in some forms of mental deficiency, also in Parkinsonism and in certain forms of paralyses, loss of cells has occurred.

To attempt to count the cells within the various nuclei individually is an almost unthinkable task, although a small number of dedicated scientists have spent their lives in studies of this sort. New scanning devices should make it possible for this counting to be done automatically, and for the mapping of the cell distribution in an entire brain specimen to be accomplished within a matter of minutes or hours. To develop an instrument for this purpose will, however, require the coordinated activities of medical and nonmedical scientists, and the expenditure of a large sum. Industry can hardly be expected to undertake the developmental cost of an instrument of this sort, of which only a limited number of units would be constructed.

Instruments are also needed for more precise analysis of the nature of nervous activity. It is not unthinkable that in the distant future some means might be found whereby artificial stimulation of the nervous system might replace the lost function of sight or hearing, or restore movement to the paralyzed individual.

Before this can be accomplished, however, precise knowledge will be necessary regarding the nature of the signals through which information is carried to the brain from the eye or ear. Further necessary information involves the modification of these messages in the various way stations through which they pass before final interpretation has been accomplished.

We have at this moment the ability to record these messages from the experimental animal, and to observe the response of the nerve and the brain to stimulation and activation of the animal.

An interpretation of the significance of these responses, however, requires analyses and computations too complicated for any but the most complex computers to carry out. Such computers are available, but their adaptation to medical problems is in its infancy.

During the past 2 or 3 years, forward-looking members of the industrial community have been turning their attention to these medical problems and offering their assistance in mobilizing their resources to attack medical problems. Such activation may be a difficult administrative problem, but could move forward medical research at a rapidly accelerating pace.

Such a program can be accomplished both through grants and direct contracts comparable to the present authorities existent for the National Institute of Mental Health's psychopharmacology program.

Proposals are in hand for programs totaling almost $1 million in this type of activity. Estimated funds needed for such a program are included in the professional judgment budget presented by NINDB for fiscal 1962.

Mr. FOGARTY. Is there anything else you want to say?

Dr. MASLAND. No.

Mr. FOGARTY. Thank you very much.

INCIDENCE AND COST OF NEUROLOGICAL DISEASES

We will place the statement on the incidence and cost of neurological diseases, and the highlights of progress in the record at this point.

(The data referred to follows:)

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases handled by the National Institute of Neurological Diseases and Blindness, and the estimated annual cost to the Nation.

I. DEATHS FROM NEUROLOGICAL AILMENTS DURING 1958 (NATIONAL OFFICE OF VITAL STATISTICS)

Category [1]	*Number*
Cerebral palsy	1,349
Cerebrovascular diseases (includes strokes and related brain ailments)	190,758
Parkinson's disease (paralysis agitans)	2,733
Multiple sclerosis	1,414
Muscular dystrophy and related ailments	559
Epilepsy	2,062
Myasthenia gravis	217
Amyotrophic lateral sclerosis	937
Encephalitis	537
Brain tumors	4,485
Total, by reportable categories	[1] 205,051

[1] The approximately 200 different neurological ailments pose unusual statistical problems. The cerebral palsy figure above includes categories 351 and 352 of Vital Statistics but not the cases found in the undifferentiated "other" of 334 Vital Statistics. Mental retardation, blindness, deafness, and speech disorders are major problems in neurology, but are not immediate causes of death. Even in the ailments for which deaths are reported, figures are unreliable because the chronically ill patient, weakened by disease, may die from an intercurrent infection and the death certificate may not record the basic neurological illness.

II. DISABILITIES FROM NEUROLOGICAL DISEASES

As the U.S. National Health Survey does not have figures on disabilities from neurological diseases, this Institute uses morbidity estimates from the respective voluntary associations stemming from known experience with cases or from surveys of a given area. Some neurological patients, such as epileptics, conceal their illness to avoid job discrimination.

Disability category:	*Total current number of disabled persons estimated*
Cerebral palsy	550,000
Mental retardation (3 percent of the population; 126,000 born annually)	5,000,000
Cerebrovascular diseases	between 1,000,000 and 1,800,000
Parkinson's disease	500,000
Sclerosing disorders:	
Multiple sclerosis	250,000
Other demyelinating diseases	250,000
Muscular dystrophy	200,000
Epilepsy	1,500,000
Myasthenia gravis	30,000
Amyotrophic lateral sclerosis	30,000
Infectious neurological disorders (including encephalitis)	over 1,000,000
Brain tumors	over 500,000
Disorder of vision:	
Legally blind	350,000
Blind in 1 eye	1,300,000
Disorders of hearing:	
Totally deaf	760,000
With major hearing and speech defects, losing between 2 and 3 million man-hours per day to industry	over 3,000,000

Disorder of speech: 2 to 5 percent of all children.

III. ESTIMATED ANNUAL COST TO THE NATION

As is self-evident, overlapping occurs with persons who have had a strike and are blind, or totally deaf; or who have Parkinson's disease and blindness; or some other combination of neurological and sensory ailments.

If, with estimated exclusions for duplication, the total of neurologically disabled persons in II is 10 million, and if minimum care per year per person is estimated at $1,000, which obviously would provide shelter care only, the cost to the country would be $10 billion. Where special diets, corrective surgery, and special medicine are used, the cost is much higher.

As mentioned in II, major hearing and speech defects cost industry between 2 and 3 million man-hours per day. At a median $2 per man-hour, the annual loss to industry is $1 billion, on the basis of a 250 work-day year.

The annual cost to the States of the 195,000 mentally retarded persons in States institutions is estimated at $250 million. No one knows the cost of supporting those in private institutions. Less than 4 percent of the 5 million mentally retarded are in institutions, public or private; the cost to individual families and communities for the other 96 percent is unknown.

For November 1960, Bureau of Old-Age and Survivors Insurance disability benefits totaled $4,502,423 to beneficiaries whose disabilities had begun in childhood. Of these disabled beneficiaries, 94 percent had neurological disabilities. Projected on a yearly basis, the cost would be over $54 million.

The Veterans' Administration does not separate compensation and pension payments in the category of neurological and psychiatric ailments. The combined figure, of which neurological payments are an important portion, is $451 million.

HIGHLIGHTS OF PROGRESS IN RESEARCH ON NEUROLOGICAL AND SENSORY DISORDERS, 1960

Items of Interest on Program Developments and Research Studies Conducted and Supported by the National Institute of Neurological Diseases and Blindness

CENTRAL NERVOUS SYSTEM

Neuraminic acid fraction in cerebrospinal fluid related to neurological disorders

Studies of a neuraminic acid fraction in human cerebrospinal fluid have resulted in findings that variations in the fraction's concentration are related to some neurological disorders. Current reports indicate that the concentration levels are significantly lower in the ventricular (brain) fluid of patients with severe cerebral edema and are increased in cases of hydrocephalus due to brain obstruction.

The effect of certain neurological conditions on the activity of the new fraction has been reported in the Journal of Clinical Investigation by Drs. L. Lahut Uzman, Edgar A. Bering, and Charles E. Morris of the Harvard Medical School.

Interest in the neuraminic acid content of cerebrospinal fluid (CSF) is founded on the possibility that variations may reflect some aspects of central nervous metabolic activity. However, no pathological processes have been correlated with such variations until recently. Initial studies by Drs. Uzman and Bering showed that neuraminic acid in CSF is composed not only of a protein-bound fraction, but of a freely dialyzable fraction (capable of passing through membranes). Unlike the protein-bound fraction, the dialyzable form does not occur widely in human serum, and is therefore capable of reflecting metabolic changes.

Previous experiments have shown that small changes in the speed of nerve impulse transmission are observed when the external longitudinal resistance is varied. However, much greater impulse transmission velocity was expected and found when the large internal resistance of the nerve was reduced by the insertion of a wire.

Giant motor-nerve fibers dissected from the squid were placed in a horizontal cell, and microelectrodes for measuring action potentials were inserted into the membrane. The transmission speed between these microelectrodes agreed with speeds reported by other studies. However, when an axial platinum wire electrode was inserted, a marked increase in conduction velocity resulted. In some cases, the time difference between action potentials recorded by the two microelectrode tips was reduced from a thousandth of a second to a few millionths of a second.

As was expected, the increase in the conduction velocity was inversely related to the surface resistance of the electrodes, so that with wires of resistances as low as 20 ohm centimeters, the conduction velocity was 230 times greater than normal over short lengths (1.5 centimeters) of axon. The investigators also concluded that the space clamp achieved by using electrodes of this resistance approaches the ideal, since the action potential is generated almost simultaneously over the entire electrode.

Study suggests different nerve impulses may use same pathways

Studies of a group of "commonsense" cells in the cat's spinal cord, which were found to respond to all skin stimuli, indicate that the traditional concept of anatomically separate sensory pathways may be modified to include systems which transmit information about more than one sensation. Reactions to skin stimuli in the cat and in man suggest that sensory messages may be transmitted along common pathways, and that the electrical discharge patterns of the central cells may determine the types of responses which occur.

Experiments which seem to confirm the theory of common-carrier pathways have been described in the *AMA Archives of Neurology* by Dr. Patrick D. Wall and John R. Cronly-Dillon, NINDB grantees at the Massachusetts Institute of Technology. The investigators emphasize, however, that both specific and nonspecific sensory pathways, as well as intermediate forms, may also exist.

These investigations were the result of the discovery of a second group of cells in the cat's spinal cord which receive messages about pain, pressure, itch, and temperature from the skin. Intracellular recording of electrical activity indicated that many primary nerve fibers converge on this cell unit. The discharge patterns of these cells were found to vary with the type of stimulus applied to the skin.

The investigators tested levels of neuraminic acid concentration in 262 patients. From this group, several smaller groups of patients with specific neurological disorders were selected. Results of these tests showed that patients with noncommunicating hydrocephalus, where the outflow of fluid from the fourth ventricle was obstructed, had a high concentration of dialyzable fraction in the brain. Lower concentrations were found when the hydrocephalus was not due to an obstruction. Similarly, fraction levels were very low in cases of spinal subarachnoid block when fluid was removed from below the site of the block. The authors suggest that this decrease may serve as a more sensitive index of physiologic block of CSF circulation than the current method of testing total protein elevation.

Patients with severe cerebral edema, regardless of cause, had a low proportion of the dialyzable fraction in the ventricular fluid. This may be due to metabolic disturbances and circulation restrictions caused by the edema, which interferes with the production of the fraction. The finding also lends support to the authors' suggestion that the new fraction is produced by metabolic activities within the brain. As expected, no correlation was found in the CSF content of either fraction in patients with chronic degenerative diseases of the nervous system.

In normal patients, the dialyzable fraction is most highly concentrated in the brain and decreases in the lower spinal region. In contrast, the protein-bound fraction is in lowest concentration in the ventricular fluid; under ideal conditions, a direct exponential relationship was found between the decrease of total protein and the increase of the dialyzable fraction. Further investigations, the authors suggest, may show this to be a useful method of approximating the neuraminic acid concentration in the brain in cases where ventricular fluid is not obtainable.

New technique speeds nerve impulses by short-circuiting internal resistance

The normal velocity of transmission of nerve impulses in the squid axon has been enormously increased through the use of low surface-resistance wires threaded along the interior of nerve fibers. By this technique, the nerve's longitudinal electrical resistance is short circuited and conduction rates may become almost infinite over the short region occupied by the wire.

The technique also provides an example of an almost perfect "space clamp." An ideally space-clamped region is defined as one over which potential changes may occur, but where the potential is the same at every point at any instant. The new finding was reported in the Journal of Physiology by Dr. J. del Castillo, formerly of the NINDB Electroencephalography Branch, and Dr. J. W. Moore of the NINDB Laboratory of Biophysics.

When the cat's skin was damaged, or when itch-producing substances were applied, characteristic high-frequency discharge patterns were recorded from the central cells. The regularity of the patterns and of the nerve impulses transmitted indicated that the pattern probably resulted from the excitation of cells in the central group which had been partially inhibited. The investigators suggest that this patterned discharge may signal the responses which subsequently occur in other parts of the nervous system. However, it remains necessary to confirm that cells in the cat are in a sensory pathway rather than in a local reflex or cerebellar pathway.

In further experiments, light vibration of the skin was found to interfere with the response of the central cells to touch, damage, itching, and temperature. The authors suggest that the vibration probably interferes with the central inhibitory mechanism, especially as decreased electrical activity was also observed when the spinal cord was stimulated directly. Parallel results were observed in man, where light vibration was found to increase the threshold for the perception of touch, pain, and temperature to a statistically significant degree.

Results of this study indicate that the newly discovered group of "common-sense" cells in the cat's spinal cord may have the ability to filter the impressions received from the skin. Thus, the filtering abilities of any cell group would determine the particular patterns of discharge that could be detected, thus enabling the cells to distinguish between the types of stimuli received.

The authors emphasize that only natural stimulation should be used to determine the nature of these filter systems, since the massive volleys from electrical stimulation do not give the cells a chance to demonstrate their ability to select, abstract, and modify the impulses.

Nervous system disorder may be etiological factor in orthostatic hypotension

Certain lesions of the nervous system, in association with an extreme drop in blood pressure when standing erect, have been observed in two patients having no systemic disease. Supported by other reports of similar cases, the study suggests that a primary "degenerative" nervous system disorder appears to be a recognizable clinical syndrome as a cause of at least some types of orthostatic hypotension.

The investigators, Dr. G. Milton Shy, Medical Neurology Branch, and Dr. Glenn A. Drager, formerly with NINDB, found the most common initial symptoms of this condition to be impotence, incontinence, and loss of sweating; "dizziness" and blurred vision occurred on rising to a standing position followed later by fatigability and the sense of muscular weakness. The signs and symptoms observed in these patients were compatible with automatic nervous system involvement and a Parkinson-like syndrome. The report appears in the AMA Archives of Neurology.

Any of the above signs and symptoms may be the presenting ones, according to the authors, and the hypotension may be a relatively late finding. Orthostatic hypotension may be present in some degree from the beginning of the illness, but usually is not detected until the patient has experienced extreme "dizziness" or syncopal attacks. The age of onset is usually in the fifties to seventies. The duration of the illness, from these cases as well as others cited in the literature, shows the disorder to be of relatively slow progression. The disorder appears to be more frequent in the male.

Within the past 5 years, the investigators have seen four clinically similar patients with orthostatic hypotension and signs and symptoms referable to the central nervous system. In the present study, pathological findings of one case are described in detail and do not appear to agree closely with pathological findings of hypoxia in the adult primate. A somewhat similar pathology has, however, been reported in hypoxic states in neonatal primates.

The authors conclude, therefore, that it is not possible, with evidence now available, to state whether the changes found in the central nervous system of this case precede the hypotension or are secondary to repeated episodes of hypoxia, but the difference in the sites of pathology suggests the former.

Origin of electrical activity in nerve cells and muscle fibers explored

A series of studies conducted by an NINDB investigator show that spontaneous, rhythmic electrical discharges occur in excitable tissues which receive no electrical energy from outside sources. The experiments suggest that the spontaneous activity may be generated by a disturbance of the intrinsic mechanism of individual nerve cells or muscle fibers. Additional studies of epileptic brain cells indicate that the same mechanism operates during seizures.

In determining the origins of electrical potentials in nerve cells in the brain, Dr. Chou-Luh Li, Surgical Neurology Branch, NINDB, found random small potentials similar to miniature endplate potentials generated from motor nerve endings. Dr. Li summarized his studies of spontaneous rhythmic activity in lectures in the Department of Physiology, University of Chicago.

In three groups of experiments, glass electrodes were used to record intracellularly from single muscle fibers. In the first study, conducted on rats with intact motor nerve supplies, no spontaneous spike activity was observed. In subsequent experiments, where the sciatic nerve of the rats was severed, the electrical potential of muscle fibers was found to oscillate continuously, often setting off a series of rhythmic spike discharges. However, the spike activity did not affect the rhythmic oscillations. Similar results were obtained in a tissue culture study of isolated muscle fibers, which were also observed microscopically.

On the basis of these results, Dr. Li suggests that this spontaneous electrical activity must be related to periodic disturbances of metabolic or electrochemical factors, which are as yet unknown, within the denervated muscle cell. Similar observations were obtained on epileptic cells in the cerebral cortex, and were reported to the Symposium on Basic Mechanisms of Epileptic Discharges sponsored by the American Electroencephalographic Society.

Biophysical studies extend knowledge of nerve membrane properties

Biophysical studies of electrical currents which cross the squid axon membrane confirm and extend the validity of theories of nerve impulse transmission which have been expressed mathematically by Hodgkin and Huxley. New data have resulted in the development of an equation which more accurately describes the characteristics of potassium ion flow through a membrane after it has been highly polarized, as well as under other electrical and environmental conditions.

A critical survey and evaluation of the Hodgkin-Huxley equations is being conducted by Drs. Kenneth S. Cole and John W. Moore, Laboratory of Biophysics, NINDB, who have reported the present study in the Biophysical Journal.

The investigators found that the original equations were valid when the membrane's electrical potential was initially at or below the resting level. When the membrane had been kept at an abnormally high potential, however, the flow of potassium ions was delayed and these equations were not applicable.

Therefore, a new formula was developed to express accurately the delayed rise of the potassium current. This expression, although more complex, was found to apply under a variety of experimental conditions. Most important, both formulas were in close agreement in situations where the original work was applicable, indicating that the underlying assumptions are probably valid.

Experiments also supported the original theories that sodium and potassium ion currents across the squid axon membrane are independent of each other. In addition, they confirmed that the potassium current pattern is dependent on a single variable, defined by a first order differential equation.

The use of mathematical expressions greatly simplifies the interpretation of highly complex direct studies of ionic membrane currents. Although these processes cannot be investigated in higher animals or man, information obtained from the large axons of squid and several other invertebrates has been found applicable to vertebrates.

BRAIN AND CEREBRAL CORTEX

NINDB study charts brain connections between cerebellum and cerebrum

Studies have confirmed the presence of nerve pathways by which the cerebellum exerts a controlling influence over the motor functions of the cerebrum. Single shock stimulation of the hemispheres of the cerebellar cortex has resulted in consistent responses in the sensory and motor areas of the contralateral cerebrum, thus demonstrating a "circuit" between these parts of the brain.

Although cerebellocerebral connections have been inferred from anatomical evidence, responses between these particular cerebellar areas and the cerebral cortex have not been demonstrated consistently. The results of a study of the connections by the evoked potential method is reported in Experimental Neurology by Dr. C. Murphy Combs and Sue V. Saxon of the Laboratory of Neuroanatomical Sciences, NINDB.

Data were obtained from 40 adult cats anesthetized with nembutal or curare preparations. Silver ball electrodes were applied to the exposed cerebellar surface and a stimulus of from 7 to 12 volts was given. Responses from similar electrodes on the surface of the cerebrum were then recorded on a cathode ray oscillograph.

From these tracings, the investigators found that the largest cortical responses could be obtained from the midsection of the anterior sigmoid gyrus—an S-shaped convolution of the motor cortex. Smaller potentials were consistently obtained from the lateral part of the posterior sigmoid gyrus. As expected, responses were much greater on the side of the cerebellar cortex opposite from the side stimulated. When responses from the same side were present, they were small, inconsistent, and occurred only in the anterior gyrus.

Early in the experiments it was observed that not all parts of the cerebellum were equally satisfactory for stimulating purposes. The most active parts of the sigmoid gyrus were then chosen as the recording point for the evoked potentials and various parts of the cerebellar surface were stimulated to determine the most efficacious stimulating points. Results of this experiment, contrary to a previous study, showed that the largest and most consistent results with the cerebellar hemispheres were obtained with low-voltage stimulation of the cerebellar area designated as crus I. The most active neocerebellar zone was found to be a longitudinal strip, bordered medially and laterally by unresponsive zones.

Electron microscopic studies of brain swelling provide clues to fluid transport

Excessive fluid within the brain, causing cerebral swelling, appears to be located solely within the clear glial cells, which may rupture in severe cases. The results of electron microscopic studies conducted by NINDB grantees also suggest that the clear glial cells, rather than intercellular space, may transport fluids in the normal brain.

The findings have resulted from detailed microscopic examinations of experimentally produced swelling in the mouse brain and of swollen cerebral tissues which surround brain tumors in man. Results were reported in the American Journal of Pathology by Drs. R. M. Torack, R. D. Terry, and H. M. Zimmerman, Montefiore Hospital, New York.

Initial experiments concerned cerebral swelling which resulted from cold injury induced by the application of carbon dioxide ice to the mouse cerebrum. In these cases, electron microscopy revealed that the fluid accumulated solely within the cytoplasm of the glial cells. To confirm these findings, additional studies were undertaken of cerebral swelling induced by other means in the mouse, as well as of swollen human cerebral tissue.

Small amounts of alkyl tin compounds added to the diets of mice (12 to 32 parts per million) caused severe cerebral swelling, accompanied by progressive neurological involvement. When the affected tissues were examined with the light microscope, however, the excess fluid seemed to be located between the cells. This finding was then contradicted by electron microscopic examination, which showed that the fluid causing the swelling was localized exclusively within the clear glial cells, and that the intercellular space was unaltered.

Similar alterations were found in human tissue obtained from the soft, rather dry, swollen area surrounding several types of intracranial tumors. Again, enlarged clear glial cells were found, and there was no intercellular fluid accumulation.

In advanced stages of tin poisoning, some of the clear glial cell membranes appeared to rupture, although fluid did not seem to penetrate the intercellular space. Human brain tissue also revealed glial cell ruptures. The wetness of the whole brain which characterizes endema may result from the increased number of cell membranes which rupture as swelling becomes severe.

According to the investigators, these studies may also indicate that the intercellular cerebral areas have little or no importance in the normal transport of fluids, as previously thought. Since the clear glial cells are clearly affected in abnormal fluid accumulation, they apparently play an important role in the transport of essential fluids within the brain.

Subcortical brain area may play role in regulating memory and recall

A subcortical brain area known as the hippocampus may govern the execution of planned motor activity by "selecting" experiences for deposit as "memory traces" in higher brain centers. Furthermore, the hippocampus may aid in recalling the experiences for use in similar goal-directed situations.

Possible functions of the hippocampus are suggested by experiments which showed significant correlations between goal-directed behavior and recordings of brain wave activity in cats. Determinations of the structural arrangement of impulse pathways in and around the hippocampus seem to support the findings. The study was conducted by Drs. W. R. Adey and C. W. Dunlop, and C. E. Hendrix, NINDB grantees at the University of California, and is reported in the AMA Archives of Neurology.

Electrodes permanently imbedded in selected areas of cats' brains recorded irregular, slow brain waves when the animals were first exposed to the test situation—a divided T-maze with a concealed food reward. However, when visual and auditory cues were provided, bursts of rhythmic slow waves occurred with each approach to the reward. As the animals learned (by successive trials) the rhythmic waves were rapidly restricted to the dorsal hippocampus and the adjacent entorhinal cortex. The rhythmic bursts persisted throughout the training period, and in late training were greatest in the entorhinal area.

Since the regular bursts occurred only shortly before and during the animal's approach to the goal and were not correlated with head and body movements, the authors suggest that the patterns are related to recall rather than to an orienting reflex. In addition, the specific burst activity disappeared when cues were not provided, but rapidly reappeared when the animal was retrained.

Electronic computers were then used to determine the sequence of brain wave activities in hippocampal and entorhinal areas. In untrained animals, impulses were found to travel from the hippocampus to the entorhinal cortex, as suggested by classical anatomical studies. In trained animals an opposite pathway was found and the hippocampus was activated by impulses from the entorhinal cortex. These results were consistent with the correlations in the previous experiments, and seem to provide structural evidence for a functional "way station" for screening incoming stimuli and for recalling memory traces.

Electron microscope studies clarify structure of secretory brain neurons

The neurosecretory system, consisting of nerve cells which secrete droplets that flow through axons to specialized organs, has been greatly clarified by electron microscope studies conducted by an NINDB investigator. For the first time, the fine structure and secretory mechanism of these cells in the brain of the goldfish has been observed. The neurosecretory cells, which are thought to supply hormones or their precursors to the pituitary body, are also found in higher vertebrates, including man.

Within the nucleus of the preoptic region of the goldfish, clusters of closely packed secretory nerve cells were found. Micrographs of individual cells showed a central zone which included multivesicular bodies and membraneous elements typical of the Golgi comlex Close by, numerous small, dense, spherical droplets enclosed in individual membranes were identified as the neurosecretory granules. Two sizes of droplets were found, 0.1 micron and 1 micron or larger, and no intermediate stage between the types was seen.

Further observations indicated that the small droplets arose primarily from the Golgi complex, whereas the larger droplets originated by gradual transformation of the multivesicular bodies. However, only the small droplet form has been found in the nerve fiber leading to the pituitary body, indicating that these granules transport hormones or their precursors. The large droplets may be concerned with such other functions as intracellular metabolism.

Results of the study were presented by Dr. Sanford L. Palay, Laboratory of Neroanatomical Sciences, NINDB, at the European Regional Conference on Electron Microscopy, Delft, Netherlands.

"Drinking" brain cells provide clues to protein metabolism and transport

Some scientists now think that certain brain cells may ingest proteins and other soluble metabolites in much the same way that amoeda surrounds and entraps its food by the movement of pseudopodia. This process, known as pinocytosis or "rinking" by the cells, has been observed in the living cells grown in tissue culture using phase-contrast optics. Otherwise, pinocytosis can be studied by tracing inclusions of protein in the cells which were made visible by labeling with a fluorescent marker.

In the various cell types of the nervous tissue grown in tissue culture, pinocytotic activity (as seen by formation of clear vacuoles in the phase-contrast optics) was closely correlated when the uptake of fluorescent proteins and was characteristic for the individual cell type. This correlation suggests that the cellular uptake of protein might take place by the mechanism of pinocytosis.

Strikingly similar protein uptake by the glial (glue) cells was observed in the area of edema surrounding brain injury in animals into whose bloodstream or subarachnoid space marked proteins had been introduced. Thus, although pinocytosis cannot be observed directly in cells in the living brain, this similarity in appearance of protein inclusions in cells grown in tissue culture to those seen in the brain suggest that pinocytotic mechanism may be active in the living brain at least under certain conditions.

This application of a technique using fluorescent proteins emphasizes the importance of the glia as a metabolic intermediary and a transmitter of substances in the brain tissue, as well as provides a technique for future investigations concerning the problems of permeability of the cerebral blood vessels to proteins. The study was conducted by Drs. Igor Klatzo and Jaime Miquel, of the Surgical Neurology Branch, NINDB, and was reported at the meeting of the American Association of Neuropathology.

CHRONIC NEUROLOGICAL DISORDERS OF INFANCY AND CHILDHOOD

"Maple sirup" disease, a cerebral degenerative condition described

A cerebral degenerative condition with onset to tonic seizures within the first week of life, and a rapid progress to death or decerebrate stage is described in Neurology by Dr. John H. Menkes, NINDB grantee at the Neurological Institute, New York City.

Ten cases of the disease, characterized by the presence of an unusual urinary odor resembling that of maple sirup, affecting four unrelated families are reported. A significant factor in the report was that pathological examination on two cases showed no abnormalities.

While the amino acid pattern at birth was found to be normal, an increased excretion of leucine, isoleucine and valine was found during later stages of the illness. An accumulation of three keto acids (alpha-ketoisocaproic acid, alpha-ketoisovaleric acid, and alpha-keto-beta-methyl-n-valeric acid) together with the absence of other metabolites along the degradative pathway of leucine suggests that oxidative decarboxylation of the alpha-keto acids is blocked in this condition. The odor of maple sirup has been attributed to the lactide of alpha-hydroxy-butyric acid.

One of the above-mentioned acids was present in the urine of a patient's mother and unaffected sister. Upon isolation it was found to be an aromatic acid of unknown structure.

Various possibilities as to the specific cause for the metabolic arrest have been examined. It has been suggested that high tissue levels of alpha-ketoisocaproic acid inhibit the synthesis of cerebronic acids.

Psychological effects of neonatal asphyxia studied in young rhesus monkeys

Behavioral changes that may result from lack of oxygen at birth have been described for the first time in a controlled group of young rhesus monkeys. Psychological tests of monkeys partially asphyxiated at birth, and of control animals delivered in a similar manner, indicate that normal animals are more emotional and more responsive to their immediate environent than are asphyxial animals. The studies were conducted by Miss Sue V. Saxon, of the NINDB Laboratory of Neuroanatomical Sciences, and the field station of perinatal physiology, University of Puerto Rico School of Medicine, and reported at a meeting of the United Cerebral Palsy Association, San Juan.

Since asphyxiation of newborn monkeys has been shown to produce neurological deficits similar to those found in some human infants, the effects of partial asphyxia on behavior and learning is currently of great interest. Previous studies of guinea pigs, conducted in the NINDB Laboratory of Neuroanatomical Sciences, indicate that nervous system damage can be directly correlated with behavorial changes.

Subjects for the primate study were six rhesus monkeys, asphyxiated by clamping of the placental cord before caesarian delivery, and five normal controls. The range of asphyxiation times in the experimental group was from 11 to 16 minutes, with a mean time of 14 minutes. When the studies were initiated, all monkeys were between 6 and 10 months of age.

In the first series of experiments, animals were placed individually in a soundproof chamber for 10-minute periods weekly for 15 weeks. Behavior was recorded at 10-second intervals and scores were based on the number of times the animal displayed emotionality, locomotion, or contact with any of the five stimulus objects in the chamber. The emotionality score was based on previously determined criteria of emotional behavior such as sucking, convulsive jerking, rocking, and crouching.

Results of this study indicated that the asphyxial subjects locomoted significantly more, tended to contact objects more, and were significantly less emotional than the normal subjects. However, near the end of the series, locomotion scores in normal monkeys increased, and contact scores in the normal group exceeded the experimental. According to the investigator, the greater emotionality in the normal group accounted for these differences, which tended to level off as normal monkeys became adapted to the observational situation.

A followup study of the same monkeys at ages 10 to 14 months partially confirmed these assumptions, since no statistically significant differences between groups in frequency of locomotion or in stimulus contact were found. Surprisingly, however, normal animals continued to be more emotional than were the asphyxial animals. In this study, each animal was observed for 3 minutes four times a day for 8 days.

The use of four stimulus conditions, ranging from an empty chamber to a complex condition (a toy bug) did not influence behavior patterns. For all of the conditions, it was found that normal animals locomoted slightly less and contacted the stimulus more often. No one emotional behavior was characteristic of any one animal or group.

In general, Miss Saxon concludes, the activity most characteristic of the animals deprived of oxygen was random or undirected locomotion. In addition, these animals did not appear to be as responsive or directed by their immediate surroundings as were the normal monkeys.

Maternal diabetes shown to cause infant abnormalities

Maternal diabetes has been further verified as one of the known conditions which may cause mental retardation and cerebral palsy in a small percentage of children. A comparative study by NINDB investigators shows that abnormalities in infants born to diabetic mothers occur about eight times more frequently than in a matched group of normal control mothers. In addition, perinatal mortality rates in diabetic mothers were found to be three times higher than in the control sample.

A detailed study, comparing the results of 235 pregnancies in diabetic and prediabetic mothers with 249 normal pregnancies, has been reported by Drs. Anatole Dekaban and Robert Baird, Section on Developmental Neurology, NINDB. The results of the study appear in the Journal of Pediatrics.

Forty-eight diabetic mothers were selected for the study from area hospitals. All were under 43 years of age, and had a history of at least two pregnancies after the diagnosis of diabetes. Normal control mothers, selected from the same hospital, were matched with the diabetic patients according to race, age, number of pregnancies, and social status. All mothers were carefully interviewed by the investigators and most of the offspring were personally examined. Children with abnormal findings were hospitalized for examination.

Although the absolute number of surviving infants diagnosed as abnormal was relatively small, abnormalities were found to occur eight times as often among infants of diabetic mothers. The abnormalities in these children included mental deficiency, congenital malformation, birth injury, and epilepsy. Total perinatal loss in the sample of diabetic mothers was 49.5 percent—three times higher than the corresponding rate in normal controls. In 78 prediabetic pregnancies (before diabetes was diagnosed), perinatal loss was 26 percent, midway between rates for diabetic and normal control mothers.

A statistical analysis of possible responsible factors showed significant correlations between outcome of pregnancy and the control of the diabetes at delivery, type of delivery, and the infant's condition at birth. The severity of maternal diabetes and the occurrence of complications during pregnancy were not statistically significant.

In the second phase of this study, a detailed analysis was made of the clinical abnormalities and pathological lesions found in the offspring of these diabetic mothers and controls. Autopsies were performed on the 18 stillborn infants and on 11 of the 13 neonatal deaths (occurring up to 4 weeks after birth). Followup studies of the six surviving abnormal children were made.

Results of postmortem examinations showed that the commonest cause of neonatal death was hyaline membrane disease, that is, the formation of abnormal membranes in the air passage. With one exception, congenital malformations found among the infants could be attributed to embryonic disturbances prior to the 10th week of gestation.

According to Dr. Dekaban, the increased incidence of birth injuries may be related to the generally oversized babies of diabetic mothers delivered at term. However, the precise etiology of mental deficiency in some children is not entirely clear and requires further study.

New nervous system disorder may be due to inherited metabolic defect

A cerebral degenerative disorder, presumably due to an error of intermediary metabolism, has been described in five boys in two generations of the same family. Distinguishing features of the new syndrome are peculiar stubby white hair, early and severe growth retardation, and severe neurological impairment, beginning soon after birth and progressing to decerebration and death. Although the symptoms and familial nature of the disorder suggest it is of metabolic origin, no specific biochemical abnormalities have yet been demonstrated.

Recent studies have shown that certain types of mental retardation or cerebral degeneration are caused by inborn errors of metabolism, although the actual extent of the problem is unknown. The recognition and identification of metabolic defects which occur with retardation is at present a promising and important field of investigation. The present study was reported at the American Academy of Neurology meeting by Drs. John Menkes and Milton Alter (formerly of NINDB), Neurological Institute, New York, and Drs. Gerd Steigleder and David R. Weakley, of the Columbia-Presbyterian Medical Center, New York. The investigation was supported by grants from the NINDB, NIAMD, and DGMS.

Two patients exhibiting the syndrome were examined by the investigators and data on three other cases were obtained from medical records and interviews. From the family history, it was determined that transmission is probably by a sex-linked recessive gene. A review of the literature confirmed that the disorder represents a clinical syndrome not previously described.

Microscopic examination showed that the stubby, coarse, white hair found in all the children was twisted, beaded, and split at regular intervals. Although cases with similar hair defects and mental retardation have been reported, none has occurred with a fatal prognosis. Additional histologic studies showed normal skin, hair follicles, and sebaceous glands.

Impairment in weight gain, severe mental retardation, and focal or generalized convulsions also occurred in all patients, and several had skeletal anomalies. Post-mortem examination, performed in two cases, revealed nerve cell loss in the cerebral and cerebellar cortex, and astrocytosis and cystic degeneration of the cerebral white matter.

Extensive biochemical studies of urine, cerebrospinal fluid, and blood were conducted to detect possible metabolic defects. However, all tests were within normal limits and no abnormal metabolites or altered amounts of normal metabolites were found. As in similar conditions where metabolic defects are suspected but cannot be defined, further study with new and improved techniques may eventually prove successful.

Study shows increase in infant deaths from hyaline membrane disease

A comparative study conducted at Johns Hopkins Hospital suggests that a recent increase in premature infant deaths from hyaline membrane disease may be related to lowered oxygen concentrations in incubators.

The incidence of fatal hyaline membrane disease in liveborn babies weighing under 5½ pounds at birth was compared for two 5-year periods, 1944–48 and 1954–58, by Drs. Mary Ellen Avery and Ella H. Oppenheimer, NINDB special trainees at Johns Hopkins University School of Medicine. Their results were reported in the Journal of Pediatrics.

An important difference between the two test periods was the change in oxygen concentration used in incubators. In 1954–58 oxygen levels were greatly reduced, since high concentrations were found to cause retrolental fibroplasia, a disease which causes blindness. During this period, the incidence of fatal hyaline membrane disease was 38.3 percent of autopsies, as compared to 24.3 percent in 1944–48, in liveborn infants weighing over 1,000 grams (2 pounds 3 ounces) who lived more than 30 minutes and less than 6 days. The incidence of the disorder for all premature infant deaths, however, increased from 21.9 percent of autopsies to 26.2 percent.

The investigators found that the disorder was rare in babies who weighed under 1,000 grams, possibly because of the structure of the very immature lung. Fatalities from the disease were most frequent in infants weighing between 1,000 and 1,500 grams. Increases in birth weights over 1,500 grams (3 pounds, 5 ounces) were associated with a marked reduction in disease incidence, which emphasizes the importance of prematurity in fatal hyaline membrane disease.

The study indicates, according to the authors, that some infants with respiratory distress may need more oxygen than they have been receiving. However, new medical techniques which allow more premature live births may also account for the increase in mortality from this disorder. In addition, the use of analgesia and anesthesia in childbirth may be a factor in the disorder and should be evaluated in further studies.

Frequent epileptic attacks in infants may cause mental retardation

Comprehensive studies by an NINDB investigator of infants suffering from frequent daily seizures have led to the hypothesis that the attacks themselves may cause retardation of development in a certain category of infants. These babies are usually under 1 year of age; their attacks are brief but very numerous, amounting to 30 to 100 or more a day; and clinical and laboratory examinations fail to reveal evidence of organic brain lesions. The last condition excludes children with brain damage in whom both epileptic attacks and retardation are caused by a common denominator—that is, some sort of cerebral damage.

Results of the preliminary study were reported in the AMA Journal of Diseases of Children by Dr. Anatole Dekaban, Section on Developmental Neurology, Surgical Neurology Branch, NINDB.

All of the six infants studied had developed normally until the onset of the frequent, but usually minor, epileptic attacks, which had begun before 6 months of age. Extensive examinations failed to show any physical or biochemical basis for the seizures, but brain wave recordings showed abnormal electrical activity in all. These and other findings suggested that idiopathic epilepsy may occur in early infancy.

A few weeks after the onset of seizures, these children displayed gradual slowing of motor and mental development, which usually was more pronounced when the attacks were most frequent. When the seizures were controlled, however, a striking but gradual improvement in development followed. The degree of improvement seemed to be related to the age of the patient, i.e., the younger the infant when seizures were stopped or diminished, the better was the prospect for his normal development.

Dr. Dekaban speculates that seizures may slow the development of initially normal infants by hampering alertness and natural ability to respond to and learn from environment. Lost learning opportunities at certain critical ages may never be fully regained. A need for a study of greater scope in this field is stressed.

Electroencephalographic patterns related to intellectual ability in brain damaged patients

A definite relationship between electroencephalographic patterns of brain damaged patients and the distribution of the patients' scores on the Wechsler-Bellevue intelligence scale has been demonstrated by an NINDB grantee.

In tests of intellectual ability in 185 patients with verified brain damage, the electroencephalographic pattern of left-sided brain damage was related to lower verbal abilities, while damage to the right hemisphere was associated with lowered scores on performance tests. In patients with generalized brain damage, no striking differences between verbal and performance scores were found.

A comparative study of four groups of patients, classified according to electroencephalographic criteria, was published in Neurology by Hallgrim Kløve the department of neurology, Indiana University School of Medicine.

Electroencephalograms (recordings of brain waves) were administered to patients referred to the Indiana University Medical Center for neuropsychologic examinations. For the purpose of the study, patients were divided into four groups, i.e., those whose electroencephalograms showed maximal abnormal activity over the right hemisphere (group I), over the left hemisphere (group II), ever both hemispheres (group III), and those with brain damage but with normal electroencephalograms (group IV). Before the groups were composed, the Wechsler-Bellevue Scale of Adult Intelligence and the Halstead neuropsychologic battery were administered to each patient.

Comparisons of Wechsler-Bellevue scores of groups I and II showed significant differences on both the performance and verbal weighted score means and on the individual subtests. Patients in group I were clearly impaired in performance areas and group II showed consistent impairment in verbal areas. However, no significant differences between performance and verbal scales were found in patients in groups III and IV, although the latter group, where electroencephalograms were normal, showed an absolute intelligence test level that was much superior to the other groups. Therefore, the author suggests, Wechsler-Bellevue results are not likely to reflect impairment in brain damaged patients with normal electroencephalograms.

Halstead's impairment index, however, failed to show any significant differences between the groups, and the indexes were found in all cases to be within the range characteristic of groups with established brain damage. Although the study was not specifically designed to evaluate Halstead's impairment index, these findings may indicate that it may be even more sensitive to brain damage than the Wechsler-Bellevue scale and the electroencephalogram.

From the results of the present study, it appears that lateralization of a brain lesion may be determined through analysis of the Wechsler-Bellevue subtest pattern. These inferences, however, are valid only if the presence of brain damage has been established and if patients are not substantially different from those used in the study.

INVOLUNTARY MOVEMENTS

Course and prognosis of acute cerebellar ataxia studied in children

New criteria for predicting the course and prognosis of acute cerebellar ataxia in children have been presented in Neurology by NINDB grantees Stuart Weiss and Sidney Carter of the Neurological Institute, New York City.

Studies of documented cases followed for periods of 9 months to 17 years indicate that contrary to previous opinions, patients afflicted with this syndrome do not always recover completely. In addition, the report suggests that severe initial manifestations may result in slow recovery.

Although the clinical syndrome of acute cerebellar ataxia has been well documented, the few followup studies to date have been of short duration and have assumed a benign prognosis. Heretofore, the clinical picture has been described as of sudden onset, often shortly after a nonspecific infectious disease, with severe gait ataxia, and complete recovery within a few months.

In this study, records of children treated for acute ataxia at Columbia-Presbyterian Medical Center were reviewed and a study sample of 18 cases selected. Of these patients, 10 recovered completely within a 6-month period after onset if illness. However, the remaining eight patients, affected with apparently the same illness, recovered more slowly, and, in some cases, incompletely.

Six of the patients—one-third of the series—showed persistent neurological deficits including gait disturbance, truncal tremor, ataxia of extremity movement, abnormal eye movement, delayed and impaired speech, and other symptoms indicative of mental retardation during followup periods ranging from 9 months to 6½ years. Impairment of speech and intellect, the authors suggest, may be due to a subtle type of cerebral involvement not detected initially.

Many factors were evaluated in all patients to determine whether the prognosis could be predicted. It was found that age at outset, race, sex, and presence of early symptoms were of no significance. The cerebrospinal fluid examination and other laboratory data obtained on initial evaluation proved of no value. However, the investigators found a definite correlation between the severity of the initial manifestations of the illness and a poor prognosis for recovery.

New knowledge relating to the possible etiology of acute cerebellar ataxia may also result from these studies. The prolonged course of the disease in one-third of the cases studied indicates that toxins, allergy, or viruses may not be causative factors. The early age at onset and the lack of new neurological manifestations over the long followup period suggest that multiple sclerosis or progressive demyelinating disease are probably not involved.

New measuring device evaluates Parkinson therapy

A new dynamic measuring device for evaluating therapy and extent of disability in patients with Parkinson's disease has been developed by an NINDB grantee at the University of Minnesota Hospital, Minneapolis. The results of preliminary tests by Dr. David D. Webster show that the technique accurately measures the effects of medication and stereotactic surgery on rigidity, strength, and tremor in Parkinson patients. The study is reported in Neurology.

The technique utilizes a powerful yet highly sensitive turntable, to which the patient's forearm is rigidly coupled by a split plaster cast. The arm is then alternately flexed and extended horizontally through an arc of 100° at various speeds. Energy required to move the forearm is automatically calculated for different rotational speeds during both active and passive motion. Unlike previous methods, the machine minimizes extraneous stimuli which may precipitate tremor in Parkinson patients.

By means of a pen writer, the system records tremors as fine as 10 grams at maximum sensitivity. In tests of strength, patients are instructed to voluntarily resist the turntable motion, and resistances as high as 90 foot-pounds may be measured. Pens also record the position of the forearm and the net work done by the turntable in moving the patient's forearm through each cycle of passive motion.

Comparisons of the test data for passive motion showed that the expenditure of energy recorded at the end of each cycle was nearly proportional to the extent of muscle rigidity. Results also showed that the maximum force required to initiate movement in the arm of a patient moderately afflicted with Parkinson's disease was twice that required to move the normal arm. In addition, the energy expended by the apparatus in moving the afflicted arm through the cycle was 10 times that of the normal. This appears to be an accurate method of measuring rigidity, since elastic muscle reactions are canceled out after each cycle.

In tests of muscle reaction to activity, a flashlight was placed in the patients free hand, and he was instructed to follow the beam of a second flashlight directed onto a screen by the operator. Although normal individuals showed no increased rigidity, this simple test was found to precipitate rigidity in patients with Parkinson's disease. Both the active and passive motion tests were used to evaluate the effects of medications and surgery on rigidity, strength, and tremor.

Responses to medication were studied by this method in several patients with varying degrees of tremor and rigidity. Because some drugs or combinations of drugs are more helpful to some patients than others, the effects of medication on the individual patient must be constantly evaluated. This technique made it possible to quickly indicate the degree of improvement or regression in response to various therapies.

At present, this technique is being used as part of a study of the effect of stereotactic surgery in Parkinson's disease. In the cases described, significant reduction in symptoms were recorded by the apparatus and clinical improvement was simultaneously observed.

Studies suggest basis for success of brain surgery in Parkinson's disease

Experiments which may explain why brain surgery relieves the symptoms of Parkinson's disease suggest that muscle rigidity and weakness may be caused by inhibition of nerve circuits between the spinal cord and bundles of muscle fibers (spindles), which promote steady voluntary contraction. Surgically produced lesions of the thalamus of the brain may reduce the inhibitory effect, thus restoring functional and balanced nerve activity.

Electrical stimulation of an area of the thalamus of the cat, investigators found, consistently inhibited afferent discharges from the muscle spindle to the spinal cord. It appears, the authors suggest, that the central nerve pathways which promote the action of muscle spindles are similarly inhibited in Parkinsonism. When the cat's muscle was stretched, the inhibitory effect was diminished; and destruction of the motor cortex abolished it entirely.

Previous studies have suggested that the activity of nerve circuits supplying the main muscle increases when spindle discharges decrease. Therefore, the rigidity and weakness of Parkinsonism may be the result of an altered balance between the two spinal cord circuits which innervate muscles. If this theory is true, surgical lesions of the thalamus reduce the inhibitory input to the muscle spindle and balance the activity of nerve circuits, with a corresponding improvement of rigidity and weakness.

The study was reported in the "A.M.A. Archives of Neurology" by Drs. Jack Stern, NINDB postdoctoral fellow, and Arthur A. Ward, Jr., NINDB grantee, of the University of Washington School of Medicine, Seattle.

NEUROMUSCULAR DISORDERS

Study yields clues to cause of familial periodic paralysis

By correlating the results of multidisciplinary investigations, NINDB scientists have clarified the nature and possible cause of a baffling neurological disorder known as familial periodic paralysis. New evidence indicates that muscle action may be disrupted by increased accumulation of fluid within the endoplasmic reticulum of muscle cells. The fluid increase may be caused by defective glycogen metabolism in muscle, resulting in an altered ionic balance.

Intensive clinical, biochemical, electron microscopic, and electrophysical studies of familial periodic paralysis have been conducted by Drs. G. Milton Shy, Theodor Wanko, Peter T. Rowley, and A. G. Engel, Clinical Investigations Unit, NINDB. A significant result is the demonstration that muscle potassium and sodium are not significantly elevated during attacks and that muscle becomes electrically unexcitable. Recording of the membrane potential by microelectrodes within the muscle cell also refutes the theory that paralysis in this disease is due to hyperpolarization by potassium accumulation.

Samples of muscle tissue obtained during attacks indicated that increased fluid was contained in large vacuoles within a specific conductive network of the muscle cell, the endoplasmic reticulum. Inside the vacuoles, granules which took up certain stains were found. This and other evidence suggests that the granules may represent the accumulation of abnormal glycogen breakdown products, which cause an influx of electrolytes and water into muscle cells to maintain ion balance.

The investigators reconfirmed that the administration of glucose, glucose and insulin, and epinepherine predisposed to attacks of weakness or paralysis. Administration and measurement of aldosterone, a potassium diuretic and sodium retention steroid, indicated that abnormal metabolism of this hormone is probably not a cause of the disease, as has been suggested. For unknown reasons, however, an excess sodium intake precipitated attacks.

Although familial periodic paralysis has been associated with hyperthyroidism, increased or decreased levels of thyroid stimulating hormone produced no adverse effects. However, low basal metabolism rates were found to aggravate symptoms, and elevated basal metabolism was associated with relief of symptoms, confirming altered metabolism of muscle as a primary defect in this unusual disorder.

The studies were presented at the scientific session of the centenary of the National Hospital, Queen Square, London.

New drugs from daffodils show promise in treatment of myasthenia gravis

Pharmacological studies to evaluate galanthamine, a drug reported by Russians to relieve some neuromuscular disorders, have resulted in the identification of a promising new series of drugs which are chemically similar but more potent than galanthamine. Studies in animals strongly suggest that the newly synthesized compounds may be effective in treating myasthenia gravis, and some are more potent than drugs now used for this disorder. Preliminary clinical trials of one of the compounds have recently been initiated.

The activity of galanthamine, its derivatives, and other chemically similar compounds in increasing muscle contraction and inhibiting cholinesterase has been evaluated by Dr. R. L. Irwin, Medical Neurology Branch, NINDB. These compounds were also compared with drugs now in use to treat myasthenia gravis. Although the cause of myasthenia gravis is not known, drugs which inhibit cholinesterase at the nerve-muscle junction usually produce striking relief of symptoms.

Initial studies showed that the drug reported by Russian scientists, galanthamine hydrobromide, was significantly less potent that the quaternary form of the compound, galanthamine methiodide. However, the latter drug was still not as effective in inhibiting cholinesterase as drugs now in clinical use, such as neostigmin.

Subsequently, the derivatives of lycoramine, which are structurally similar to galanthamine, were tested on muscle for the first time. Two of these derivatives were found to be more potent than neostigmin, although their toxicity was greater. A third compound was less toxic than neostigmin, yet was more active than pyhysostigmine. It also had a slower onset of action than the other derivatives and was absorbed after oral administration. At present, the third derivative seems to be the most promising for clinical trial.

Both the galanthamine and lycoramine compounds are particularly interesting because they differ chemically from drugs currently used to treat myasthenia gravis. In addition, they can be obtained from the bulbs of plants in the amaryllis group, such as the daffodil, which are readily available throughout the world. The specific compounds tested by Dr. Irwin include: galanthamine hydrobromide, galanthamine methyl iodide, lycoramine methyl iodide, deoxylycoramine methyl iodide, deoxydemethylycoramine methyl iodide, lycoramine acetate methyl iodide, neopine, and neopine methyl iodide.

The results of the studies were presented at the meeting of the American Society of Pharmacology & Experimental Therapeutics, Seattle.

Progressive skull changes observed in hereditary muscular disorder

An NINDB study has confirmed that "hyperostotic" skull changes are a variable finding in dystrophia myotonica, an inherited type of muscular dystrophy. Of 18 patients with the disease, skull changes were observed in the X-rays of 17 (94 percent) by Drs. G. Di Chiro and J. E. Caughey, Neuroradiology Branch, NINDB. Observations suggest that the changes are progressive and that they may be related to increased growth hormone activity.

Four types of radiographic changes in the skull vault were defined: thickened calvaria throughout, thickened calvaria in the frontal region, irregular bulgings of newly formed bone in the frontal region (hyperostosis frontalis interna), and thickened calvaria throughout with hyperostosis frontalis interna. Changes of the vault appeared with equal frequency in males and females, although previous studies have shown that cranial hyperostosis occurs almost exclusively in women.

The most marked skull changes were found in patients afflicted with the disease the longest. In addition, the degree of change was greatest in eight patients with confirmed gonadal failure, suggesting that the unrestrained activity of growth hormone may be a cause of the progressive skull alterations. The study appears in "Acta Radiologica."

MULTIPLE SCLEROSIS

Allergic encephalomyelitis quantitative index developed

A quantitative index correlating the clinical signs and severity of lipemia with histologic lesions has been developed to aid in assayng encephalitogenic activity of brain extracts.

By studying accumulated data on a large number of animals injected with brain or active chemical fractions of nervous tissue, Dr. Ellsworth Alvord, NINDB grantee at Baylor University College of Medicine, and Dr. Marian Kies, Research Branch, National Institute of Mental Health, Bethesda, developed the index. A description of their work appears in the Journal of Neuropathology and Experimental Neurology.

Many attempts have been made to demonstrate the activity of various chemical fractions of brain in producing encephalomyelitis when injected parenterally with adjuvants. Although decreasing doses to determine the threshold or 50-percent-effective dose have been used for whole brain, only one similiar study has been made with various fractions of brain in a search for the causative factor or factors.

Approximately 1,000 healthy adult male guinea pigs were used for the study. Following an initial observation for 2 weeks, groups of 10 animals were injected intradermally with vaccines containing various amounts of brain or brain extracts in Freund's adjuvant. After 30 days, survivors were anesthetized, blood collected, and the animals killed by perfusion intracardialy. Clinically positive animals were sacrificed when they had developed unquestionable signs of the disease. The brain and spinal cord were removed for neuropathologic examination. Clinical signs, degree of lipemia, and degree of histologic changes were coded according to severity. It was observed that lipemia practically did not occur except with the combination of severe clinical and histologic changes. Correlations between these three factors were then made, first considering all of the possible subdivisions, and subsequently combining various subdivisions which did not appear to be significantly different from each other.

By plotting the mean numerical index of the severity of the experimental disease against the weight of material injected, a curve was obtained demonstrating the severity of the disease produced by different doses of the particular material. The dose that produced 50 percent of the maximal severity of the disease was termed ED_{50} (50-percent-effective dose) and could be used as a single index of the effectiveness of the particular substance injected. A close approximation to the ED_{50} was made by using the dose that produced a disease index of 4; this was chosen because the average maximum disease index was about 8 (on a scale ranging from 0 to 10). In this way whole guinea pig brain was compared with bovine spinal cord, cord acetone powder, lipid-free residue of cord, water soluble, 5 percent KCL soluble, and water-insoluble residue of cord as to comparative activities in producing experimental allergic encephalomyelitis in guinea pigs. Of all of these, the 5-percent KCL was the most active material per unit weight. It was approximately 6 times as active as lyophilized guinea pig brain and 10 times as active as lyophilized bovine spinal cord. The assay is being used to study the isolation and purification of the compound or compounds in the central nervous system responsible for producing the disease.

"Allergic" encephalomyelitis in guinea pigs suppressed with brain extract

For the first time, experimental "allergic" encephalomyelitis induced in guinea pigs has been suppressed by administration of the same chemical component which most effectively produces the disease. Allergic encephalomyelitis in animals (EAE) is histologically similar to a number of demyelinating diseases in humans, and has been linked with such disorders as postvaccinal and postinfectious encephalomyelitides, and acute multiple sclerosis.

The important discovery was the surprising result of experiments initiated to test skin reactions to encepholitogenic vaccines which are known to cause the disease in animals. The findings were reported by Drs. Cheng-Mei Shaw, Wilson J. Fahlberg, and Ellsworth C. Alvord, Jr., NINDB grantees at Baylor University College of Medicine, and Dr. Marian Kies, Research Branch, National Institute of Mental Health, Bethesda, and appear in the Journal of Experimental Medicine.

Although prevention by pretreatments has been reported, suppression of EAE by treating animals previously injected with disease-producing vaccines has been demonstrated only once. In the similar study, whole brain rather than isolated fractions was used.

To induce the disease, the investigators prepared vaccines of whole homologous brain extract and killed tubercle bacilli in water-in-oil emulsion (Freund's adjuvant technique), which were injected into the skin of guinea pigs. Skin-test solutions of acid extract of defatted guinea pig brain were then administered at intervals. Suprisingly, animals repeatedly skin tested at 11, 15, 21, and 28 days after injection of vaccines did not develop significant clinical or histologic evidence of the disease. Further studies were then initiated to determine whether the suppression was real or a statistical artifact, and whether it was use to the tuberculin, to the brain extract, or to some nonspecific stress reaction.

In conducting the study, 50 to 80 white male guinea pigs were injected with encephalitogenic vaccine, and subgroups of 5 to 10 animals received skin-test solutions on predetermined days after initial injection. Each animal, including uninjected controls, was observed daily for evidence of disease. After 30 days, survivors were sacrified and brain and spinal cord were examined. In addition, animals were scored according to a graded "disease index" and an average disease index was obtained for each group for statistical analysis and comparison.

Although the investigators found no significant results when 0.5 milligram of acid extract was given on the 11th and 15th days, there was almost complete suppression when five such injections were given on each of the 9th, 14th, and 21st days. Additionally, larger doses were found to produce more complete suppression of the disease, indicating a quantitative relation to the time of administration and the dose administered. A non-specific-tress situation, produced by intradermal injections of 20 percent alcohol, did not affect the disease. Furthermore, the effects of tuberculin were statistically insignificant and inconsistent.

At present, the etiology and pathogenesis of "allergic" encephlomyelitis is unknown. However, some clue may be afforded by the finding that a more active extract is more effective, suggesting that the suppression is due to a specific desensitization, defection or neutralization of antibodies, or paralysis of antibody forming mechanisms. The absence of skin reactions in both injected animals and in controls, however, indicates that an immunologic process is not involved.

Further experiments on this complex disease reaction are necessary to determine if the suppdession is due specifically to encephalitogenic extracts, as constrasted to nonencephalitogenic, and to elucidate the mechanism of the suppression.

Geographic variation in prevalence of multiple sclerosis verified

An epidemiological survey conducted in two comparable, but widely separated, communities showed that the prevalence of multiple sclerosis is 2.4 times greater in Halifax County, Nova Scotia, than in Charleston County, S.C. The survey was conducted by a single team of investigators who used uniform screening, classification, and diagnostic procedures.

The two communities were selected for the survey because they are similar in population, size, area, medical facilities, and are Atlantic seaports. They differ, however, in racial composition, geographic latitude, and climate.

Identical predetermined criteria were used to screen provisional cases, which were then classified by category. The same team of investigators personally examined most patients in both communities.

Results showed that prevalence rates per 100,000 inhabitants based on clinically acceptable cases, were 13.8 in Charleston and 32.3 in Halifax. For the white population alone, the prevalence was 1.7 times greater in Halifax, and no preponderance of cases was found to be characteristic of any ethnic group.

Further investigations revealed no factors which accounted for the prevalence differences. Age distribution of patients was similar in each community, as were clinical and genetic manifestations of the disease. The age-specific prevalence rates were higher in Halifax in almost every age group.

Drs. Milton Alter and Leonard T. Kurland, Epidemiology Branch, NINDB; Dr. R. S. Allison, Royal Victoria Hospital, Belfast, Northern Ireland; and Dr. O. Rhett Talbert, Medical College of South Carolina, Charleston, reported their findings in World Neurology. This new journal also contains a report of a related NINDB-supported study, coauthored by Dr. Kurland, which indicates that the prevalence of multiple sclerosis may be less in Japan than in North America or Western Europe.

Patterns of nerve demyelinization directly observed in tissue culture

A new approach to demyelinating disorders such as multiple sclerosis has been developed by NINDB grantees who have induced and studied nerve demyelinization in tissue culture. Serum from animals with experimental "allergic" encephalitis (a condition resembling certain human demyelinating diseases) was found to produce patterns of demyelinization in cultures of newborn rat cerebellum. No such reaction was obtained after treatment with blood serum from normal animals or with antikidney serum.

The serum is toxic only to brain tissue, as cultures prepared with liver, muscle, and peripheral nerve tissue did not react to it. The rapidity of the reaction indicated that the response is probably not due to an infectious process.

The response begins with pronounced swelling of the neuroglia cells and myelin sheaths. Often, fragments of myelin sheaths are extruded into surrounding areas. Both the fragments and the sheaths then rapidly disintegrate and are converted into small fat granules. Neuron cell bodies and axis cylinders are left intact, just as they are in demyelinating disease.

Possible further applications of the tissue culture model have been suggested by Drs. Murray B. Bornstein and Stanley H. Appel, NINDB grantees at Mount Sinai Hospital, New York, who reported the findings at the American Academy of Neurology meeting.

Mechanism of biosynthesis of long chain fatty acids described

The detailed sequence of biochemical reactions for the formation of long chain fatty acids in the cells of living animals has been described for the first time by an NINDB investigator. Fatty acids combine with glycerin to form fats, and are essential components of myelin, the fatty nerve sheath which degenerates in such disorders as multiple sclerosis.

In studies with purified enzyme systems from liver and brain, Dr. Roscoe Brady, Laboratory of Neurochemistry, NINDB, has shown how acetic acid, a 2-carbon unit, is converted to a 16-carbon chain fatty acid known as palmitic acid.

Early studies conducted by Dr. Brady and other scientists established that the presence of carbon dioxide was essential for fatty acid synthesis. Subsequent work by Dr. Brady indicated that the key intermediate in the biosynthesis is a derivative of malonic acid, known as malonyl coenzyme A.

As a result, Dr. Brady was able to synthesize malonyl coenzyme A by adding carbon dioxide to acetyl coenzyme A, a derivative of acetic acid. By labeling these compounds, he discovered that 1 molecule of acetyl coenzyme A and 7 molecules of malonyl coenzyme A, combined with 14 atoms of hydrogen, are required to build a molecule of palmitic acid.

The steps in the synthesis are as follows: When acetyl coenzyme A combines (condenses), the newly added carbon dioxide is displaced. When two atoms of hydrogen are added, the resulting compound can condense with another molecule of malonyl coenzyme A. This process is repeated until the appropriate chain length is reached.

To identify the intermediates which participate in these reactions, the required enzyme systems were isolated and purified. Each step in the sequence of reactions leading to fatty acid synthesis was defined by radioactive labeling of synthetic intermediary compounds. This basic finding, which has been presented, will be reported in the Journal of Biological Chemistry, and may aid in the understanding of metabolic defects associated with diabetes and degenerative disorders of the nervous system. The study will also be described to the International Biochemical Congress(Symposium on Lipid Synthesis) in Moscow, U.S.S.R., in August 1961.

AMYOTROPHIC LATERAL SCLEROSIS

Possible cause of spinal cord disease demonstrated by NINDB grantee

An experimental disorder, similar to some human virus infections and degenerative disorders of the nervous system, has been produced in cats injected with 5-fluoroortic acid (FO), a pyrimidine analog which was found to interferen with the production of nucleic acid in nerve fibers. These studies suggest that similar metabolic disturbances may occur in some diseases affecting the gray matter of the spinal cord, such as amyotrophic lateral sclerosis.

Functional and structural disturbances produced by FO in the nervous system, as well as preliminary biochemical studies of its action, have been reported in the AMA Archives of Neurology by Dr. Harold Koenig, NINDB grantee at Northwestern University Medical School. Subsequent biochemical work was reported at the annual meeting of the American Academy of Neurology.

Intrathecal injection of FO in cats was found to produce two independent neurological disorders. The initial disorder, a neuronopathy, affected the neurons, or spinal gray matter; the second, which appeared several weeks later, was a leukomyelopathy, affecting the white substance of the spinal cord. Clinical signs of neuronal irritation, similar to those occurring in many progressive diseases of gray matter in man, appeared 1 or 2 days after injection, causing spontaneous contractions of muscle fibers, myoclonic jerks, and augmented muscle tone and reflexes. If the neuronopathy was sufficiently severe, loss of neuronal function ensued, characterized by a flaccid paralysis with loss of reflexes and severe muscle atrophy.

Pathological changes were confined to the gray matter for several weeks, and consisted of a progressive depletion and disruption of the Nissl substance (protein bodies in the cytoplasm of nerve cells). According to Dr. Koenig, this was probably due to impaired biosynthesis of ribonucleic acid (RNA) in nerve cells. This was then confirmed by biochemical studies where radioactive carbon atoms were added to FO. Autoradiographic studies showed that the compound was effectively incorporated into the RNA of neurons and oligoglia—tissues which surround the nerve's myelin sheath. Derivatives of FO were found in the acid-soluble fraction and RNA of neural tissue, indicating that efficient anabolic conversion had taken place.

Therefore, says Dr. Koenig, FO probably causes neurological dysfunction by producing defective coenzymes and abnormal RNA molecules, thus altering the normal mechanism of protein synthesis. Eventually, such interference brings about a depletion of RNA in the spinal cord.

After the second week of illness, a spongy degeneration of white matter in the spinal cord appeared, associated with more severe neurological changes. Dr. Koenig suggests that this is due to a blockage of DNA synthesis, with a resultant inhibition of cell division in the oligoglia. Defective proliferation of the oligoglia may play a similar role in the spongy degeneration of white matter which occurs in pernicious anemia.

Other pyrimidine analogus tested produced no notable neurological effects, initially verifying that the changes were caused by specific metabolic disturbances. Biochemical studies further clarified this theory, since labeled carbon studies showed the impairment to be due to conversions of FO which interfered with nucleic acid biosynthesis. The degree of protein inhibition was found to parallel closely the severity of the neuronopathy.

EPILEPSY

Mechanisms underlying experimental epileptic seizures described

Repetitive, self-sustained electrical discharges from brain cells, very similar to those taking place during human epileptic seizures, may be caused by a slow process of cellular repolarization, which occurs after the cell membrane has been excessively depolarized by repeated electrical stimulation.

In an experimental approach to the problem of epilepsy, Dr. Paul Gerin, former guest worker in the Electroencephalography Branch, NINDB, systematically analyzed spike patterns elicited by repeated electrical stimulation of brain cells. An interpretation of the mechanisms which may cause afterdischarge, that is, self-sustained activity which follows repetitive electrical stimulation, has been published in the Archives italiennes de Biologie. Afterdischarge is very similar to spontaneous seizures recorded from the exposed cortex of epileptic patients, and is often used as a tool for experimental study of epileptic activity.

Electrical stimulation of varying strength, frequency, and duration was applied to the cerebral cortex of adult cats with bipolar silver electrodes. The activity of single cells during and after stimulation was recorded by means of tungsten microelectrodes and by larger electrodes on the surface of the cortex. Of a total of 2,500 afterdischarges elicited, 600 were accompanied by visible spike activity and were recorded on film. Detailed analysis was made of activity in 80 different cortical cells.

Repeated stimulation, Dr. Gerin found, was usually accompanied by progressive and characteristic changes in the size and frequency of spike activity elicited by each electric pulse. When these changes did not occur, the phenomenon of afterdischarge rarely developed. Changes included a tendency for units to discharge repetitively and progressive decreases in the amplitude of spikes until activity sometimes ceased entirely.

When the spike firing ceased entirely, self-sustained electrical activity (afterdischarge) usually occurred, characterized by small, high frequency spikes, which progressively increased in amplitude and decreased in their rate of firing. The self-sustained activity eventually ceased when the spikes returned to the prestimulation level of amplitude.

According to Dr. Gerin, spike changes during and after stimulation may be ascribed to changes in polarization levels in the cell membrane. Thus, during repeated stimulation, recovery of the resting polarity level cannot occur, and a progressive depolarization of the membrane results. When this depolarization exceeds a critical level, firing stops and, during the process of cell repolarization, self-sustained activity develops. Although conducted on an experimental level, these studies suggest that this unusually slow process of repolarization might be the characteristic feature of "epileptic" neurons.

Brain-wave pattern correlated with that found in brain tumor patients

An electroencephalographic (brain wave) pattern, which frequently occurs in patients with idiopathic petit mal epilepsy, has also been found, with statistically significant frequency, in patients with brain tumors. Detailed findings of two cases where tumors were associated with this EEG pattern and an extensive review of similar cases indicate that the abnormality which produces the typical "petit mal" pattern may lie within the brain stem. Unlike many other types of epilepsy, seizures which show this pattern usually cannot be correlated with gross or microscopic lesions in the brain.

Among the most striking and typical in clinical EEG, these brain-wave recordings are characterized by bilateral, symmetrical 3/second wave-and-spike complexes. Studies relating this pattern with pathological findings were reported by Dr. C. Ajmone-Marsan and Dr. W. R. Lewis, NINDB Electroencephalography Branch, at the Eastern EEG Association meeting, Ste. Marguerite, Quebec, Canada.

In the two cases examined by the investigators, both EEG's showed the typical pattern, highly suggestive of petit mal epilepsy. In the first subject, a large metastasis of one cerebellar hemisphere was found, but the patient had no history of epileptic seizures. In a second case, the patient demonstrated petit mal, as well as temporal lobe epilepsy and generalized convulsion. Here, a large astrocytoma extending into the thalamus was removed from the right temporal lobe.

Because cases of brain tumors associated with bilateral 3/second wave-and-spike paterns are so rare, statistical evaluation was devised to assure that a valid relation existed between the two phenomena. The respective incidence of brain tumors and of the "petit mal" pattern were calculated for the general population. Results showed that if chance alone were operating, an association of the two factors would occur in 48.2 out of a million cases. However, data from three published reports totaling 1,071 brain tumors resulted in an "actual" frequency of 6 cases, as compared to an expected occurrence of 0.0517 case on the basis of chance. According to the investigators, this discrepancy is significant enough to warrant the conclusion that the phenomena are related.

The predominant extracortical, midline location of brain tumors in the cases examined as well as in all similar cases reported in the literature suggests that the brain stem plays a significant role in the production of this very characteristic, yet still mysterious, EEG pattern.

Brain-wave pattern may be means of locating epileptic lesions

A characteristic pattern of brain-wave activity has been found by NINDB grantees to monitor the onset of both penicillin-induced and spontaneous epileptic seizures in man. Since this pattern, unlike the isolated. interictal spikes, is sharply localized to the epileptic focus, its detection should be useful for locating epileptic lesions during surgery.

The phenomenon of "afterdischarge" had been described in humans by Drs. Bruce L. Ralston (formerly of NINDB) and Christos A. Papatheodorou, NINDB grantees at Mount Sinai Hospital, New York. Their report appears in Electroencephalography and Clinical Neurophysiology. These findings confirm Dr. Ralston's previous experimental studies in cats and monkeys, which showed that full seizures developed from similar afterdischarges rather than from progressive increase of interictal spike frequency.

Brain-wave recordings directly from the cortex of animals (electrocorticography) indicated that penicillin applied to the brain was capable of eliciting afterdischarge, followed by fully developed seizures. As a result, experiments were initiated to determine if similar activity existed in human convulsive disorders.

Since spontaneous seizures are rarely recorded during electrocorticography and electrically induced seizures are of a somewhat different type, penicillin was also used as an activating agent in man, prior to cortical surgery. The investigators found that the rapid, low-voltage afterdischarge could be easily elicited, and that it also could progress to fully developed seizures. Although the frequency of occurrence of the phenomenon is not yet known, no seizures were seen to develop through a simple increase in spiking activity.

Examination of a patient with temporal lobe epilepsy confirmed that such afterdischarge is also a characteristic of spontaneous seizure activity. In this case, the afterdischarge pattern was observed to occur at the same time as the abdominal sensation (epigastric aura) which often precedes epileptic seizures.

According to the authors, the recognition of afterdischarge may be of practical importance, because unlike spike patterns, which are often projected widely from their original area. the afterdischarge tends to remain clearly localized to the epileptic focus. Thus, it should prove a valuable means of determining the primary epileptic focus for surgical removal. In addition, these studies clarify the still unknown mechanisms of seizure formation in man by defining more precisely the changes which the electrical activity undergoes during the development of an epileptic seizure.

Brain's water and electrolyte balance related to seizure susceptibility

The high susceptibility of young animals to convulsions due to fevers—febrile seizures—has been ascribed by an NINDB grantee to an immaturity of the balance of water and electrolytes (solutions which conduct electrical impulses) in the brain. Studies in animals show that susceptibility to febrile seizures can be increased or decreased by experimentally altering the brain's water and electrolyte balance. Observations of conditions which influence seizure susceptibility in children suggest that the findings may be clinically valid.

Investigations of the relationship between susceptibility to febrile seizures and age were conducted by Dr. J. Gordon Millichap, NINDB grantee and special trainee at the Albert Einstein College of Medicine, N.Y., and are reported in "Neurology." Initial studies by Dr. Millichap demonstrated that the height of the temperature at which seizures occur may be used as an accurate index of seizure susceptibility.

To identify the mechanisms which may influence seizure threshold, hyperthemia was induced in groups of newborn, 1-month-old, and adult rats, and convulsive temperatures for each group were determined. Water and electrolytes in palsma and brain tissue were then examined in rats of the same age and strain, and results were correlated with seizure susceptibility in the corresponding groups. In the young animals, a significant correlation was found between high susceptibility to seizures and high intracellular water content of the brain. These susceptible animals were also found to have high levels of extracellular potassium and low levels of extracellular sodium.

To confirm these findings, the water and electrolyte balance in adult rats was experimentally altered to approximate that of the young rats, by such procedures as overhydration and glucose administration. When this was done, significant increases in seizure susceptibility occurred.

Clinical studies of children subject to febrile seizures suggest that similar changes in the water and electrolyte balance may be present. In addtiion, states of overhydration or salt depletion have been found to lower seizure thresholds in both children and adults.

Chemical patterns in the brain used to classify drug-induced seizures

Studies by NINDB grantees have demonstrated that certain types of cerebral seizures may be distinguished on the basis of specific chemical patterns in the brain, even though the electrographic patterns are alike. Although some chemical changes in the brain occur with all intense convulsions, other changes were found to be specific for the type of convulsive agent used. A tentative classification based on chemical patterns has been outlined for drug-induced seizures.

New data on seizures induced by four convulsive agents have been reported in "Neurology" by Drs. William E. Stone, Jean K. Tews, and Ellis N. Mitchell, University of Wisconsin Medical School. Changes in brain chemistry occurring during seizures were determined in dog cerebral tissue frozen in situ. Analysis of some 15 cerebral chemicals led the investigators to classify these seizures into the following types.

The first chemically distinct type were seizures induced by anticholinesterase drugs. These seizures are recognized by the accumulation of acetylcholine in the brain. In addition, atropine was found to block this type, but not to affect any of the other types studied.

Seizures induced by fluoro-fatty acids, specifically fluoroacetate and fluorobutyrate, were also accompanied by specific changes in brain chemistry. Here, inhibition of the enzyme aconitase resulted in an accumulation of citrate in the brain, and large amounts of ammonia were also present.

A third possible category are seizures caused by picrotoxin and pentylenetetrazol. Although chemical changes were similar for both of these drugs, no major effects were found which accounted for their convulsive action. Convulsions due to pyridoxine deficiency represent another distinct type. Deficiencies of pyridoxine probably cause seizures by inhibiting the formation of gamma-aminobutyric acid in the brain.

Although many other known convulsants, such as strychnine and methionine sulfoximine, may cause specific chemical changes, additional studies with these compounds are necessary. The determination of chemical changes associated with induced seizure activity in animals may be of importance in defining some causative factors and possible therapies in human epilepsy.

HEADACHE

Humoral agent implicated in vascular headache of migraine type

An extremely powerful vasodilator, labeled "neurokinin," has been found in the body fluids of patients during severe and long-lasting vascular headache of the migraine type. In addition to the neurokinin, the body fluids contained an enzyme capable of forming neurokinin, termed neurokinin-forming enzyme (NFE). The increased content of these substances found locally could account for the pain associated with headaches of this type.

This clinical study, conducted by Drs. L. F. Chapman, A. O. Ramos, G. Silverman, H. G. Wolff, and Helen Goodell, B.S., at the New York Hospital-Cornell Medical Center, is reported in "AMA Archives of Neurology."

During the painful phase of these attacks, the authors report, there is dilation of the large and small blood vessels of the head both intra and extracranially, often more on one side than the other. In most attacks, however, the pain stems chiefly from the large subsurface cranial arteries and their branches and aching pain is experienced when these vessels are distended, pulled upon, or displaced.

Intradermally injected tissue fluids containing mixtures of neurokinin and NFE induce pain, lower pain threshold, increase capillary permeability, and heighten vulnerability to injury. Also, the release or activation of neurokinin-forming enzyme and subsequent formation of neurokinin has been observed during neuronal excitation in man in a variety of circumstances. The potent hypotensive and vasodilator action of this substance and its formation during neuronal excitation suggest strongly that it serves in local vasomotor control for the nervous system and is also linked to migraine headache attacks.

CEREBROVASCULAR DISEASES

Factors underlying recurrent cerebrovascular attacks described

Many recurring cerebrovascular attacks may be attributed to the failure of anastomotic small blood vessels attempting to compensate for stricture or occlusion of a major cerebral artery. Their failure may be caused by a variety of events including lowered systolic blood pressure, local hypertension, anomalous vascular distribution, and inadequacy of other major cerebral vessels.

A report by Dr. D. Denny-Brown of the Harvard Medical School in the "AMA Archives of Neurology" suggests that analysis and treatment of factors which cause cerebrovascular episodes should precede anticoagnulant or surgical therapy, and further definition of these causes may result in beneficial therapeutic measures.

Initial studies by Dr. Denny-Brown showed that recurring, temporary episodes of partial paralysis, formerly attributed to vascular spasms, were caused by a phenomenon which he called carotid or basilar insufficiency. This syndrome occurs when a stricture or occlusion impedes the blood flow of one or more major arteries. Arterial function is then taken over by collateral, or secondary arteries. Impairment of the collateral circulation at this time, however, was found to result in a hemodynamic crisis, usually temporary and reversible, but which caused anatomical damage when severe. Hemodynamic crises occurred most frequently in patients with low systolic blood pressure, high blood viscosity, and anemia.

Subsequent studies were designed to investigate physiological factors which might cause the collateral circulation to fail and thus precipitate hemodynamic crises. In these experiments, the oxygen content of tissues in the monkey brain was measured by polarograph electrodes or stereoscopic microscope. Findings showed the occlusion of carotid or cerebral arteries caused an immediate drop in blood supplies to the area, with a resulting decrease in oxygen levels. Although the oxygen loss in normal animals was very great at first, it tended to rise slowing, reaching a high or moderate recovery level.

Following carotid occlusion, when the monkey's blood pressure was lowered by withdrawal of blood, the small collateral vessels at first dilated, but quickly became constricted. The slow flow of blood resulted in the appearance of a phenomenon called venous microstasis, characterized by clumping of red cells and stoppage of blood flow (stasis) in the very small venules. Although venous microstasis could be reversed by an increase of blood pressure, it resulted, if untreated, in microscopic intracortical hemorrhages, with a related death of affected nerve tissue.

The occurrence of venous stasis in the human brain is also related to low systolic blood pressure. In man, however, vascular occlusion may be incomplete, although the collateral insufficiency produced may result in considerable disturbance of function. Once a severe episode has occurred, attacks may cease, due to the decreased oxygen requirement in the affected tissues.

In managing cases of cerebrovascular insufficiency, therefore, it is essential to insure adequate blood pressure levels and oxygenation of arterial blood to prevent failure of the collateral circulation. Although anticoagulant therapy may be useful in preventing the initial clumping of red cells, this treatment has little subsequent effect.

Arterial spasms observed in hypertensive monkeys, while not related to insufficiency, were found to prevent adjustment in the collateral circulation. Unsuspected damage to the vertebral arteries in the neck has also been demonstrated to cause compensatory failure.

Recurrent, temporary cerebrovascular episodes may occur, however, in the absence of an insufficiency syndrome. Such cases, Dr. Denny-Brown suggests, may be caused by soft, friable emboli, probably composed of platelets and fibrin, which temporarily constrict blood vessels. Such platelet clumps, which appear to result from previous damage to a blood vessel, have been observed in experimental animals, and should be suspected when slight, frequent attacks occur. Although these clots have a natural tendency to fragment and disappear, anticoagulant therapy may in these cases have a beneficial effect.

Treatment for cerebrovascular insufficiency, Dr. Denny-Brown suggests, should be designed to counteract the immediate cause of symptoms. In the majority of cases he has observed, causative factors have been defined, and correction has been satisfactory in 50 percent without anticoagulant therapy or surgery. Although such therapy is of value in some cases, a thorough analysis of possible causative factors should be made before undertaking treatment.

New syndrome of circulatory insufficiency in spinal cord described

Temporary deficiencies of blood supply in the spinal cord, in patients with damaged blood vessels of the cord, have been studied and recognized as a syndrome similar to circulatory insufficiency of the brain. Although less common, the syndrome has been described in patients with spinal artery occlusion who exhibit episodic fluctuation of neurological symptoms. In addition, the investigators found that symptoms in these cases were temporarily aggravated by smoking.

The first definitive studies of transient vascular insufficiency of the spinal cord were conducted by Dr. C. Van Buskirk and M. Davidson, NINDB grantees at the University of Maryland School of Medicine, Baltimore, and were reported in the Southern Medical Journal.

Symptoms of occlusion of the anterior spinal artery, which usually occur abruptly, include partial paralysis, sensory loss, and possible muscular atrophy. However, patients usually show some degree of recovery, indicating that collateral, or secondary, circulation gradually substitutes for the damaged artery. In three cases studied, impaired collateral circulation in the damaged portion of the cord resulted in a temporary insufficiency syndrome, characterized by transient fluctuation of symptoms.

Since symptoms in two patients were temporarily aggravated by smoking, animal experiments were initiated to study the effect of nicotine on the spinal circulation. Intravascular injection of nicotine in dogs was found to effect a significant, although temporary, reduction in spinal cord circulation. Thus, the authors conclude, the temporary neurological symptoms which occurred in patients after smoking resulted from the reduction by nicotine of the already impaired circulation.

In treating patients with spinal artery insufficiency, it is necessary to promote the collateral circulation and prevent its failure. Previous studies have suggested that the same factors influence spinal cord blood flow as influence cerebral circulation. Therefore, treatment should be aimed at insuring adequate cardiac function, avoidance of drops in blood pressure, intensive physical therapy, and a consideration of anticoagulant therapy. The investigators suggest that anticoagulant therapy be initiated only in carefully selected patients with a firmly established diagnosis.

Normal occurrence of connective tissue in CNS described

Strands of connective tissue fibers attached to adjacent blood vessels of the brain and spinal cord have been found in normal animals of 12 species, although many investigators have associated the fibers only with pathologic conditions. The recognition of the normal and widespread distribution of intervascular fibers will prevent erroneous diagnoses of such disorders as capillary fibrosis (where vessels are occluded by hyperplastic connective tissue fibers). In cerebral edema, however, stretching of these fibers may be a cause of impeded blood flow in small vessels.

Stained sections of brain and spinal cord tissue from normal animals were compared microscopically by Dr. J. Cammermeyer, Laboratory of Neuroanatomical Sciences, NINDB. Findings were reported in the Journal of Comparative Neurology. Intervascular fibers were found to vary in size, number and distribution in different species and locations. Strands were innumerable in the pigeon; they were numerous and prominent in the dog, raccoon, monkey and cat; and less numerous in the rabbit, guinea pig, chinchilla, rat, hamster, squirrel, and mouse. No strands were found in the opossum, which has no capillary network.

Evidence that these fibers are derived from blood vessels is based on their staining qualities, intimate connections with vessels, and arrangement. Modification of the blood flow with normal maturation may result in regression and atrophy of scattered blood vessels, leaving connective tissue fibers bare.

The function of these fibers is not yet clear, except that they act as a support for the brain's vascular system. However, they should be considered in such pathological conditions as edema, where stretched fibers may constrict blood vessels. The high prevalence of intervascular strands in the spinal cord may also influence studies of the etiology of diseases of the cord.

Effects of occlusion of small cerebral arteries demonstrated experimentally

Studies of traveling blood clots in small arteries on the surface of the brain show that tissue damage occurs only if a branch of the artery which penetrates the cortex is occluded. If the clot does not lodge on a penetrating artery, complete occlusion of the surface (leptomeningeal) artery can occur without tissue disintegration (infarction) or breakdown of the natural barrier between blood and brain.

In conducting the experiments, NINDB grantees at the Bowman Gray School of Medicine, Winston-Salem, N.C., injected a steel sphere into a large artery of the dog brain, and localized it in a surface artery. Thus, the effects of a single, uniform point occlusion, where other vessels are unaltered, could be determined.

Drs. J. Kiffin Penry and Martin G. Netsky found that blockage of a penetrating artery characteristically caused two major, well-defined infarcts: one in the gray matter of the cortex, the other deep in the central white matter. The location and appearance of these infarcted areas was similar in each brain examined.

This phenomenon, they suggest, may be due to the structure of the brain's collateral, or secondary, circulation. In the penetrating arteries, the small capillary connections are not sufficient to compensate for the occluded vessel. Tissue damage in the gray matter may extend only to a depth where larger collateral vessels are located. But a sparseness of capillaries in the white matter again results in an area of damage.

The investigators noted that the infarct in the cortex was of a red, or hemorrhagic type, implying that a damaged blood-brain barrier allows a leakage of capillary blood cells. The deeper infarct was white, or anemic, possibly because of the poorer capillary supply. In previous studies of humans, a combination of red and white infarcts was attributed to the movement of a clot through the artery. But the steel sphere, which could be localized with certainty, was always located above both areas of damage.

Complete blockage of vessels without infarction has been described in other organs (such as the heart) in cases where the occlusion developed slowly. Yet occlusion in the dogs was sudden, necessitating an immediate development of collateral circulation. Although the collateral circulation of the leptomeningeal arteries of dogs has been shown to be similar to that of man, the authors indicate that occlusion of the same vessels in a human brain with atherosclerosis or arteriosclerosis might produce severe and irremediable damage. These findings were reported in the Archives of Neurology.

DISORDERS OF VISION

Side effects of enzyme used in cataract surgery evaluated

Alpha chymotrypsin, an enzyme which facilitates cataract surgery by fragmentation of the fibrils in the suspensory ligament of the lens (zonula fibers), is found to injure the endothelial lining of rabbit corneas, although the damage is usually temporary. This injury does not seem to be of a specific nature. Related studies show, for the first time, that endothelial cells multiply by mitosis, or indirect division.

The report of an NINDB committee investigating the use of alpha chymotrypsin was presented by Dr. Ludwig von Sallmann, Chief, Ophthalmology Branch, NINDB, at the annual meeting of the American Academy of Ophthalmology and Otolaryngology. The report summarized the findings of a cooperative study suggested by the academy to investigate the effects of the enzyme on other parts of the eye.

In studies by Dr. von Sallmann, alpha chymotrypsin was infused into the anterior chamber of the eye of young rabbits, and removed after 3 minutes with washings of 0.9 percent saline solution. Subsequent examinations showed that the corneal endothelium was frequently injured. In some of the experiments, varying degrees of corneal clouding were found to occur. In these instances, large defects of the endothelium could be detected microscopically. Damage confined to a small area usually disappeared after 24 hours, although extensive corneal clouding sometimes persisted for more than 5 weeks. Control animals infused solely with 0.9 sodium chloride also occasionally exhibited endothelial damage.

Because of the difficulty of examining the endothelium, a new technique was devised in which the entire cell population of this tissue could be studied. Flat mounts of the whole endothelium were prepared by dissecting layers of the excised corneas under a stereomicroscope. A significant result of this technique was the demonstration that cells in the endothelium of adult animals multiply by mitosis, contrary to previous assumptions that division was amitotic, or by direct cleavage. In animals with extensive injuries, cell regeneration by mitotic activity was greatly increased.

Results of preliminary tests of the allergic effects of alpha chymotrypsin, conducted by Dr. G. van Alphen of the Ophthalmology Branch, NINDB, were included in the report. Here, guinea pigs were sensitized by repeated injections of the enzyme. Challenge doses a month after sensitization did not produce noticeable allergic responses. These studies may indicate that adverse reactions to alpha chymotrypsin are unlikely to occur in patients previously treated with the enzyme for other disorders, or where it is used a second time for a cataract operation.

Also described were electromicroscopic studies of the effect of alpha chymotrypsin on the lens conducted by NINDB grantees A. P. Ley, A. S. Holmberg, and T. Yamashita of the Washington University School of Medicine, and reported in the American Journal of Ophthalmology. The investigators found that the zonules, supporting structures of the lens, are fragmented into uniform segments 3 to 5 minutes after alpha chymotrypsin is administered. These experiments, conducted with monkey and human eyes, contradict previous findings that the enzyme merely weakens the fibers of the zonules.

Venous circulation of intact living eye viewed by new technique

The application of an intricate radiographical technique to intact living eyes has enabled an NINDB investigator to describe the complex intraocular venous circulation of the cat eye. Little known anatomical details and theories of circulation, which may be applicable to human eyes, have ben clarified by the use of this technique.

Although radiographic methods have been used to study the vascular system of the living brain, the valuable tool previously had not been applied successfully to the vessels within the eye. Known as intraocular venography, the new technique is of potential value in diagnosing some eye disorders and in studying such conditions as congestive glaucoma, in which vascular disturbances occure. The study, by Dr. Bruce E. Cohan of the NINDB Ophthalmology Branch, was reported in A.M.A. Archives of Ophthalmology.

In performing the experiments, the anterior ciliary vein of the cat was exposed, divided, and cannulated with a needle attached to tubing and a syringe. The vein was then perfused with a radiopaque material and film packets were placed flat in a space provided by the removal of the cat's nasal orbital wall. During perfusion, exposures were made by appropriate positioning of a central X-ray beam.

An interpretation of these radiographs enabled Dr. Cohan to design a schematic composite of the circulation patterns and to describe little known details of the intraocular venous system. Since other comparative studies have shown that the intraocular circulation of the cat and dog resembles that of man, Dr. Cohan suggests that the findings of this study may be valid for the human eye.

Radiographic evidence failed to confirm the presence of previously described swellings and constrictions in the veins of the choroid, a vascular layer between the sclera and the retina. It is possible, however, that the elevated venous pressure during the experimental procedure obscures such caliber changes which might be present under physiologic conditions. In addition, high-speed perfusion resulted in the appearance of radiopaque material in the anterior aqueous chamber—between the cornea and the iris—implying a connection between the chamber and the intrascleral veins. The intrascleral veins were also found to communicate with the veins of the ciliary body, which connects with the iris.

The study showed that when perfusion rates were increased, intraocular pressure also increased substantially. In several experiments air was not completely flushed from the tubing and harmless amounts were introduced into the circulation. The finding that large amounts of air were trapped in the vortex sinus when intraocular pressure was elevated suggested that outflow from the vortex vein had been impeded. According to Dr. Cohan, this tends to confirm the many speculations that venous outflow is strangled under conditions of elevated intraocular pressure.

New concepts of drug action in lowering intraocular pressure reported

A surprising correlation between venous and intraocular pressure in the eye has been described as a result of a new technique for experimentally measuring these pressures without altering the relationship between them. Studies have shown that Diamox (acetazolamide), a drug used to lower intraocular pressure in glaucoma, produces parallel decreases in both intraocular and venous pressure in the cat eye. Diamox was also found to act selectively, without interfering with the general blood pressure.

A description of the experimental technique and subsequent studies of the effects of Diamox on the eye were presented by Dr. Frank J. Macri, Ophthalmology Branch, NINDB, at the meeting of the American Society for Pharmacology and Experimental Therapeutics.

Preliminary to the drug study, casts of the aqueous outflow veins of the cat eye were made to demonstrate connections with the systemic veins. The effect of Diamox was then measured by simultaneously recording the aqueous pressure in the anterior chamber and the venous pressure in the anterior ciliary or one of the vortex veins. Continuous measurements were made before, during, and after the administration of the drug.

In previous studies, eye and venous pressures had not been determined simultaneously. Thus the venous pressure was essentially determined on an occluded vein while the eye pressure was obtained under conditions of an unimpaired circulation. A technique was, therefore, devised where either the anterior ciliary or the vortex pressure was measured simultaneously with the intraocular pressure and the blood pressure. The comparative experiments showed that no changes in the eye's "responsiveness" resulted from the cannulation of veins for purposes of measurement.

When Diamox was administered intravenously, expected decreases in eye pressure occurred. In addition, simultaneous decreases in eye venous pressure were recorded, which were parallel to intraocular changes in time of onset and in magnitude. In addition to performing the experiments in living animals, studies were made or isolated arterially perfused eyes. Similar correlations of intraocular and venous pressure were found under this condition and Diamox was still effective in lowering these pressures. Since under these conditions decreases may be ascribed to the alkalinity of the drug used, a comparable buffered solution was administered by continuous perfusion to the isolated eyes. Lack of pressure decreases under these conditions confirmed that Diamox acts directly on the eye.

Intraocular pressures in 1 eye of each of 39 cats were then plotted against corresponding venous values before and after Diamox administration. Decreases after the use of Diamox were statistically significant for all cases. A significant linear correlation between venous and eye pressures was found, a relationship which was unchanged by the use of the drug. According to Dr. Macri, this finding could indicate that the vasculature plays a role of greater significance in the maintenance of ocular pressure than has been attributed to it in the past.

Although no conclusions are warranted relating to the mechanism by which Diamox causes the venous pressure to fall, two possibilities are indicated. Venous pressure may decrease as a result of lowering the eye pressure, since Diamox is known to decrease aqueous inflow. Or intraocular decreases may be due to falls of venous pressure, implying that some mechanism produces a lessened blood volume. Further studies on these intricate phenomena may contribute to the understanding of intraocular pressure regulation.

Improved method for diagnosing malignant tumors within the eye reported

Isotope tracer methods for detecting malignant ocular tumors have been implemented by NINDB investigators who have devised criteria for successfully applying these methods to tumors in the posterior half of the eye. Tracer methods that are used to locate tumor sites in the front of the eye have previously been ineffecive in locating posterior tumors. The improved method for localizing tumors in the posterior chroid has been reported in the AMA Archives of Ophthalmology by Dr. J. O'Rourke, formerly of the NINDB Ophthalmology Branch, now at Georgetown University, and Eleanor Collins, NINDB.

Eight patients, each with evidence of a tumor beneath the retina in the posterior half of the eye, were studied. Radiophosphate was administered intravenously to the patients 24 hours before uptake measurements were made. Beta emissions were counted for 1 minute in each of four posterior and anterior quadrants of the eye. After the tumors were excised, pathologic sections were examined to determine the cell type and volume of each tumor.

Results showed that the routine anterior counting procedure localized the posterior malignancy correctly in only one of eight cases, and the average radioactivity of the tumor was only 25.3 percent above the mean of individual quadrant counts. In six cases where the new criteria were used for posterior countings, the tumor was located correctly in all instances. The average increase in tumor radioactivity was 74 percent above the mean. The investigators also found that tumors larger than 300 cubic millimeters and those with epithelioid cells (which are associated with high malignancy) retained greater amounts of radioactivity. However, factors such as density of overlying tissue made it difficult to equate tumor size with radioactivity emitted.

As a result of these findings, the authors propose that different methods be used to detect posterior malignancies than are now used for locating ocular tumors. They suggest that 1-minute counts of quadrants in both the front and back hemispheres of the eye be made, and that posterior counts be taken from bare sclera, following surgical exposure and muscle detachment. A positive diagnosis of a posterior tumor can be made if the total radioactivity in the back hemisphere exceeds the total anterior values by more than 40 percent. Radioactivity detected over the tumor site should also exceed the mean of posterior counts by more than 40 percent. In addition, the point of highest radioactivity should correspond with the site of retinal detachment.

This method of detecting posterior malignancies is highly accurate since more radioactivity can be counted, thereby reducing the chances of error. In addition, the actual area which the tumor has invaded can be more accurately determined. The technique will also be of value in advancing operating time, since the difficulties previously encountered in detecting posterior malignancies often delayed surgery.

NINDB studies clarify role of nerve pathways in regulating eye pressure

Sensory neurons in the eye which respond to increased intraocular pressure are not involved directly in the maintenance of normal eye pressure in the cat. In addition, NINDB studies have indicated that, over short periods of time, intraocular pressure is not regulated by the central nervous system. Although the existence of a neural center which regulate eye pressure has been suggested to explain clinical observations, a reflex pathway has never been demonstrated.

To determine if such pathways exist, investigators recorded the afferent impulses—from the eye to the brain—from the ciliary nerves of the cat, which carry the sensory nerve fibers of the eye as well as its autonomic supply. Experiments were conducted on isolated, perfused cat eyes, and findings were confirmed in intact, anesthetized animals.

In both types of experiments, no spontaneous neural activity was observed which could be related to normal intraocular pressure levels. Increases in pressure, however, resulted in increased activity of the larger sensory fibers of the long ciliary nerves. The impulses evoked by raising the pressure, suggest the authors, may be due to the stretching of nerve fibers in the outer coats of the eyeball.

Indirect evidence for central regulation of intraocular pressure also was sought in intact animals. Stimulation of the third and fifth cranial nerves (which give rise to the ciliary nerves) was found to produce transient changes in eye pressure. However, when the normal pressure was increased by infusion of fluid into the eye's anterior chamber, no changes in the efferent activity—from the brain to the eye—were observed. In addition, blocking the nerves by local anesthesia did not affect the normal pressure or the response to small imposed changes of pressure.

In view of these findings and of the small amount of activity evoked by pressure changes, the authors conclude that short term regulation of intraocular pressure in the cat is probably not a function of the central nervous system. However, the study does not exclude the role of neural activity in regulating normal eye pressure, since the techniques used did not permit the study of the activity of small fibers or of long-term changes in pressure. The study was conducted by Dr. P. P. Lele, formerly of the NINDB ophthalmology branch, and now at Massachusetts General Hospital, and Patricia Grimes, ophthalmology branch, and is reported in Experimental Neurology.

Visual adaptation to the dark depends on recovery of pigment

A study which shows how human eyes adjust to the dark after exposure to light, conducted by an NINDB ophthalmologist, has proven that dark adaptation is directly related to the regeneration of a photosensitive pigment in the retina known as rhodopsin or "visual purple."

Further conclusions substantiate findings from animal studies indicating a linear relationship between recovery of night vision and regeneration of rhodopsin, regardless of differences in light exposure (bleaching) or subsequent time in the dark.

An ingenious method for measuring both dark adaptation threshold (point of minimum vision) and rhodopsin levels in the same eye has been developed by Dr. W. A. H. Rushton, former visiting scientist, Ophthalmology Branch, NINDB, who reported the results of this work at the meeting of the Association for Research in Ophthalmology. By this method, predetermined fractions of rhodopsin in specified retinal regions can be bleached with lights of varying intensities, and the extent of bleaching and rhodopsin recovery can be measured by retinal densitometry, which determines pigment density.

In typical experiments, different intensities of rhodopsin bleaching, ranging from total to 25 percent, were produced and studied. The subject alternated between the densitometer and an apparatus for measuring dark adaptation, which employed yellow and green filters to indicate the point of transition from cones (day vision) to rods (twilight vision). In all cases, the point of transition and the return of minimum vision occurred when rhodopsin was about 90 percent regenerated.

Dr. Rushton concludes that the dark adaptation threshold is probably dependent on the fraction of "opsin," a chemical component of rhodopsin, which has not at a given time combined with "retinin," a yellow pigment, to form rhodopsin. This theory is supported by electroretinographic studies in animals which indicate that the amount of rhodopsin remaining after bleaching or vitamin A deficiency has a linear relation to the level of the visual threshold.

VERTIGO

Destructive therapy evaluated for relief of incapacitating symptoms of Miniere's disease

Incapacitating symptoms of Meniere's disease affecting one ear can be relieved by a simple and effective surgical technique known as the transtympanic labyrinthotomy. This technique, which destroys the function of the inner ear, is recommended only when medical therapy fails to prevent recurring and severe attacks of the disorder.

The criteria for undertaking destructive therapy and for determining the appropriate surgical or drug technique are examined by Dr. Harold F. Schuknecht, NINDB grantee, associate surgeon, Division of Otolaryngology, Henry Ford Hospital, Detroit, in an article published in the AMA Archives of Otolaryngology.

Dr. Schuknecht cautions that destructive therapy should be considered only when Meniere's disease is conclusively diagnosed, when the vertigo and nausea are incapacitating, and when medical regimens fail to provide symptomatic relief.

When destruction is indicated, and hearing in the healthy ear is good, unilateral involvement may be treated effectively by surgical transtympanic labyrinthotomy, or, as Dr. Schuknecht suggests, by intratympanic streptomycin injection. Since these procedures result in hearing loss in the diseased ear, existence of a progressive disease in the other ear must be ruled out.

Destructive therapy by either technique is not recommended unless the threshold loss for speech reception is at least 40 decibels and the speech discrimination score is not better than 40 percent.

According to Dr. Schuknecht, the surgical method is simpler and quicker. The intratympanic streptomycin treatment, which the investigator first tried on a series of cats before its use on humans, causes patient discomfort and requires daily injections for a week. Its only real advantage is that it requires no general anesthetic. Destruction of vestibular function by either method must be complete, otherwise the disease will persist in the residual sense organs.

Where the disease affects both ears—only in about 10 percent of the cases—the technique employed should assure preservation of the existing hearing. Because of its remarkable selectivity, parenterally administered streptomycin sulfate assures the safest destruction of the labyrinth without impairing auditory sense.

Dr. Schuknecht stresses that pretreatment audiograms and quantitative caloric tests should be given at frequent intervals beginning 10 days before starting outpatient treatment, with particular emphasis upon caloric results. Injections to a point just short of total destruction of the vestibular system have been found by Dr. Schuknecht to produce optimum relief while avoiding the prolonged ataxia. To assure careful observation, the patient should be hospitalized after a week of outpatient treatment. It will be helpful to the patient to understand the nature of the temporary posttreatment disability—principally ataxia—which will gradually improve.

Dr. Schuknecht concludes that carefully administered parenteral streptomycin therapy can effectively relieve incapacitating symptoms of bilateral Meniere's disease. In cases of unilateral involvement, however, an equally effective result can be achieved by surgical ablation with less subsequent vestibular upset.

PROGRAM HIGHLIGHTS

New developments in NINDB's collaborative perinatal project

For the past 4½ years, including 2½ years of intensive preparation and pretesting, NINDB has directed a long-term collaborative research attack on cerebral palsy, mental retardation, and other neurological and sensory disorders of infancy and childhood. The project is the first large-scale effort to collect information on the many factors which may cause neurological and sensory disorders. It is also the first large research program to collect detailed information during pregnancy, labor, delivery, and the early life of the child rather than after disorders occur.

The project will eventually involve some 50,000 pregnant women and their children in all parts of the country. Working on the project at 15 private hospitals and universities are obstetricians, pediatricians, neurologists, and specialists in at least a dozen other medical and related scientific disciplines. Their common objective is to determine whether there is a relationship between the events and influences present during pregnancy, labor, delivery and the first month of life, and the later appearance of neurological or sensory disorders in some cases.

Since the main phase of the project was started in January 1959, there have been three major developments. First, a strong and closely knit organization of the 15 collaborating institutions and the central office has been forged. Second, the procedures for collecting data on the pregnant women and their children have been improved. And third, the number of women and children enrolled in the project has steadily increased: by the end of October 1960, study records had been received on about 12,274 mothers and 6,725 children.

Perinatal research exhibits displayed

To describe NINDB's collaborative project, two new scientific program exhibits, entitled "The Fateful Months When Life Begins" and "40,000 Mothers and Their Babies," were prepared this year and shown at the annual meetings of 15 professional societies.

The exhibits provide brief statements of the relationship between conditions affecting parents and the occurrence of abnormalities in their offspring, as well as some of the etiological factors which may result in deviations in pregnancy outcome.

Puerto Rico primate studies enter fourth year

Major scientific contributions relating to the developing nervous system and oxygen deficiencies at birth have resulted from primate studies conducted by NINDB's Laboratory of Perinatal Physiology, Puerto Rico. Now in its fourth year of operation, the project has acieved its initial objective by establishing conclusively that monkeys asphyiated at birth develop symptons which resemble mental retardation and cerebral palsy. Current research is aimed at developing means of prolonging survival of asphyxiated monkeys and preventing resulting brain damage.

The studies are designed to complement the aims of the Institute's collaborative project on perinatal pathology in humans. At present, scientists are producing asphyxia in monkeys under more standard conditions, and investigating the numerous physiological changes which result. New observations have been made of brain pathways over which nerve impulses travel. Behavioral studies have shown marked differences between animals born and reared in captivity and those in the free-ranging colony.

Related accomplishments include the standardization of neurological examinations for newborn monkeys, establishment of normal growth and development patterns, descriptions of structural changes in the brains of asphyxiated monkeys, and important observation of behavior and learning activities.

The Puerto Rico facility has been made available to several other scientific groups in this country and abroad, including other NIH Institutes, for collaborative or individual studies. Outstanding studies conducted by Dr. Geoffrey Dawes and others, Nuffield Institute for Medical Research, Oxford, England, have obtained for the first time accurate records of the oxygen supply of the fetus, which has wide implications for causes of fetal suffocation in the human. Plans are being made to allow other interested investigators to use these animals and facilities for primate research, and to develop the laboratory as a center for experimental studies of numerous adverse conditions which may cause neurological disorders.

Maternal and child care mission to the U.S.S.R.

The second NINDB-sponsored mission of six American scientists to the U.S.S.R. has surveyed Soviet progress in the field of maternal and child care.

The 30-day tour was part of a scientific-cultural exchange program between the United States and the Soviet Union. A group of Russian specialists will make a similar study of maternal and child care in this country at a later date.

Members of the U.S. delegation were Drs. Stewart H. Clifford, Boston Lying-In Hospital; Allan C. Barnes, Johns Hopkins Medical School; Katherine Bain, Children's Bureau, DHEW; B. G. Greenberg, University of North Carolina; Edith Potter, Chicago Lying-In Hospital; and Fred S. Rosen, Children's Hospital, Boston.

A report which details the findings of the first NINDB-sponsored medical exchange mission to the Soviet Union has recently been published. It contains observations on Soviet research activities in the physiology and pharmacology of the nervous system by six scientists who toured Russian research institutions in 1958. Copies of the extensive report (PHS publication No. 800) are available on request from the NINDB Information Office.

Advisory group formed to study needs in cerebrovascular research

To aid in outlining and implementing a national research program in cerebrovascular diseases, NINDB early in the year appointed seven neurological scientists to serve as a Cerebrovascular Program Advisory Group.

Before recruiting manpower and stimulating research on a national scale, the group has delineated the role of the neurological scientist in the study of vascular diseases of the brain. They have indicated that a major problem in the vascular field is the interpretation and measurement of the harmful effect of vascular disease on the organ concerned. They recommended that the "primary role in devising, implementing, and evaluating all forms of research in cerebrovascular disease must reside in the collective disciplines known as neurological science." A resolution to this effect was adopted by the National Advisory Neurological Diseases and Blindness Council as part of its policy in cerebrovascular research.

Progress reported in aneurysm study

An accelerated pace has been reported in NINDB's Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhages, begun early in 1958 and scheduled to be completed in 1962. The study, designed to give certain basic information and to point out lines for future research activities, is acquiring a large reservoir of clinical data.

Although specifically directed toward the analysis of subarachnoid hemorrhage and aneurysm, this accumulation of data is pertinent to and potentially available for the study of many facets of the general problem of cerebrovascular disease.

By the middle of 1960, the study had compiled a total of 1,000 reports of subarachnoid hemorrhage, 450 of which have been proven to be caused by intracranial aneurysms.

When a sufficient number of cases have been reported, the project will determine which clinical types of patients suffering from aneurysms are best suited for particular medical and surgical therapies, and favorable sites for surgical removal of aneurysms.

Varying opinions result from anticoagulant study

Results of NINDB's cooperative anticoagulant project, which began late in 1957, indicate that the use of anticoagulant drugs is certainly feasible, but may involve definite risks and problems. The aim of the project is to evaluate the usefulness of anticoagulants in preventing "little strokes," in warding off the occurrence or recurrence of major attacks, and in reducing the neurological deficit which may result. A study at one cooperating institution concluded that anticoagulant therapy did not substantially affect mortality from strokes, whereas another study has indicated that anticoagulant therapy is beneficial in treating certain types of cerebrovascular disease.

A future study will compare the effects of anticoagulants alone with anticoagulants plus fibrinolytic agents. Previous studies compared anticoagulants with controls.

International conference on vascular disease of the brain

Research progress and future needs relating to vascular disorders of the brain, including findings from NINDB cooperative studies, were outlined by international authorities who attended a 2-day conference in Miami. The conference, jointly sponsored by the NINDB Advisory Council and the American Academy of Neurology, followed the annual meeting of the AAN, and was attended by over 500 scientists. Reports were presented by investigators from the United States, England, Canada, France, Belgium, Denmark, and Sweden.

The proceedings of the conference will be examined in detail by a selected group of authorities to determine the areas which would benefit from initiated or expanded research.

Planning of international cerebrovascular study supported by grant

A research grant for the planning of an international study of the epidemiology and neuropathology of strokes was awarded by NINDB to the World Federation of Neurology with headquarters in Antwerp, Belgium. The Federation, an international professional organization, will enlist the cooperation of its 48 member societies in conducting the study.

The project proposes to investigate factors which cause strokes in different national, ethnic, racial, and cultural groups throughout the world. During the planning phase, uniform reporting methods will be developed to evaluate lesions in the vessels of stroke patients. Means of selecting uniform patient samples must also be determined, so that results of studies in different countries can be meaningfully compared.

At a conference in Antwerp, study participants and the Advisory Group agreed upon tentative operating protocols that have been developed to standardize study results. They recommended that a central laboratory be established for uniform interpretation of specimens from cooperating institutions. To initiate the pilot study, the group suggested that methods be devised to begin collecting specimens at research centers in Oslo, Norway, and Turin, Italy. Arrangements will be made to evaluate institutions in other countries for inclusion in the study.

First international symposium on Parkinson's disease cosponsored by NINDB

Fifty-one of the world's foremost authorities on Parkinson's disease, convening at Arden House, concluded that a central registry of Parkinson victims would facilitate systematic study and analysis of the ailment. Highlighting the 3-day symposium, the first international event of its kind, were the findings of five specialized panels, presented at an open meeting.

New estimates of the prevalence of Parkinson's disease were presented, with the estimate that 1 out of 40 Americans, or 2.4 percent of the population, will develop the disorder. At present, some 34,000 new cases are reported in this country annually.

The current deficit in knowledge of Parkinson's disease was attributed in part to the lack of standardized approaches and of uniform terminology. In addition, too many Parkinson cases are treated without careful study or are not reported. Participants agreed, however, that an immediate step toward eventual eradication would be the establishment of a complete registry of case histories, to be available to scientists everywhere, for study and analysis in the search for possible causes, prevention, and cures.

Differing opinions relating to the merits of surgical therapy were presented, as well as basic knowledge of nerve connections within the brain. In addition, the neurologists agreed that most drugs now in use for relieving Parkinson symptoms are generally unsatisfactory. Summary opinions were also developed by the symposium concerning possible hereditary factors in Parkinson's disease, the location of brain impairment, or malfunction, and the experimental production of the disease in animals.

Drug therapy in neurological and sensory disorders evaluated at national symposium

Higher and more uniform standards for clinically testing drugs for neurological and sensory disorders were discussed at a symposium, sponsored by the NINDB Advisory Council, at the University of Wisconsin. One hundred outstanding neurologists met with eight of the Nation's leading biostatisticians to set up standards for clinical trials of drugs now in use, as well as for future therapy.

Panel groups in eight specific disorders reviewed the broad aspects of therapy and proposed methods for most effective evaluation of drugs in each disease area. Sessions were held to discuss epilepsy, glaucoma, multiple sclerosis, vertigo, Parkinsonism, headaches, muscle diseases, and neuropathies and neuralgias.

Preceding the panel meetings, objectives of the symposium were outlined and the importance of human clinical trials in screening proposed drugs was emphasized. The clinical neurologist was advised to cooperate with experts in designing and evaluating experimental trials. The general session also included talks by representatives of the pharmaceutical industry and the Food and Drug Administration who defined problems in testing and evolving new drugs.

The symposium was highlighted by reports summarizing the findings of the eight specialized groups. Specific recommendations relating to the design of clinical drug trials in each area were presented. In general, the participants concluded that additional work in this essential area was imperative. They also agreed that methodology studies should be undertaken to develop accurate and consistent definitions and categorizations of disease entities to be studied, to validate available methods of examination of patients and to establish uniform criteria of drug effectiveness.

Cooperative study on glaucoma detection continues

An NINDB-supported cooperative study to evaluate methods for screening and diagnosing glaucoma has entered its second year at four research centers throughout the Nation. Techniques currently applied to the detection and identification of glaucoma are being evaluated at the Wilmer Institute, Johns Hopkins University Hospital, Baltimore; the Moffitt Eye Hospital, University of California Medical School, San Francisco; the Department of Ophthalmology, State University of Iowa, Iowa City; and the Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo.

A report on a glaucoma family study, undertaken by NINDB grantees at the latter university, appears in the October 1960 issue of the American Journal of Ophthalmology. In a 12-month period, 110 siblings, children, and parents of known glaucoma patients have been studied.

Glaucoma studies presented in award-winning exhibit

Relationships between the severity of eye chamber angle changes in glaucoma and of certain systemic disorders are illustrated by an NINDB grantee exhibit which was awarded the Hektoen Gold Medal at the annual meeting of the American Medical Association in Miami Beach. The medal is awarded on the basis of originality and excellence of presentation for an exhibit of original investigation.

The exhibit is entitled "Chamber Angle Anomalies in Developmental Glaucoma and in Systemic Mesodermal Disorders." It presents findings indicating that certain connective tissue disorders, such as Marfan's syndrome and idiopathic scoliosis, are consistently accompanied by abnormalities in the connective tissue of the eye's chamber angle. These abnormalities are structurally similar to chamber angle anomalies in the two basic types of developmental glaucoma, suggesting that the conditions may have a common cause.

Also illustrated are microscopic and histochemical studies which indicate that both the systemic disorders and chamber angle anomalies may result from inborn metabolic errors that cause weakening of the ground substance supporting connective tissue cells and fibers.

The Hektoen Gold Medal was presented to Drs. Hermann M. Burian, Gunter K. von Noordon, Ignacio V. Ponseti, and Mr. Edwin Lee Allen, of the State University of Iowa College of Medicine, Iowa City.

Pilot study of uveitis organized

In a new approach to the problem of uveitis, leading ophthalmologists attending an NINDB-supported conference on this disorder organized and initiated a pilot study for analyzing records of uveitis patients. The initial study, which will include some 500 case histories, will be used in organizing a larger project to be conducted at 4 major eye clinics. Analysis of numerous case histories may provide a basis for determining possible causes, means of prevention, and cures for the blinding disease.

Conference participants also evaluated a proposed classification system for uveitis and retinitis. To determine its practical value, they suggested that the system be used for a year by clinicians working in these disease areas. Dr. Alson E. Braley, of the State University of Iowa, a member of the NINDB Advisory Council, was chairman of the conference.

Effects of radiation on the nervous system evaluated at international symposium

The response of the nervous system to ionizing radiation was discussed by 42 authorities from 7 countries (including Russia) at a symposium at Northwestern University, jointly supported by NINDB and the Atomic Energy Commission.

Five half-day sessions, each followed by a discussion period, covered the effects of radiation on the developing nervous system, particle irradiation (particularly the use of high energy rays in neurosurgery), and histopathological, functional, and psychological changes resulting from radiation exposure. Dr. Ray Snider, an NINDB grantee at Northwestern, was chairman of the symposium, which was attended by some 340 scientists.

Differing opinions relating to the effects of low dosage radiation were presented. Studies indicating that a very low radiation level produced congenital abnormalities in embryo rats were reported by Dr. Roberts Rugh of Columbia University. Low dosage radiation was also reported to increase the incidence of audiogenic seizures in affected mice. Another study, reported by Dr. Orville T. Bailey, University of Illinois, a member of the NINDB Neurology Postgraduate Training Committee, suggested that observed effects of radiation on the nervous system are primary, rather than secondary, to vascular changes. This observation confirms the study of Dr. Milton Brightman, Laboratory of Neuroanatomical Sciences, NINDB.

A paper presented by Dr. Marcel Monnier, of Basel, Switzerland, revealed that low doses of radiation altered electrical discharge patterns in the brains of mice. Other reports concerned the necessity for exact definition of radiation sensitivity, the relation of age and species to radiation damage, and the effects of radiation on nerve impulse transmission. Participants also reported that, in general, motivation and motor activity are decreased by radiation exposure.

Research opportunities in chronic disease hospitals

The research potential in chronic disease hospitals throughout the Nation was considered at a 2-day NINDB conference attended by 30 directors of research, superintendents of hospitals, and chiefs of neurology.

The agenda included a review of the present patient load, types of patients, and disorders involved. Participants were urged to outline types of research opportunities within their institutions and to suggest ideas for their fullest possible exploitation.

Consideration was given to unique conditions existing in certain chronic disease hospitals for the study of controlled populations over extended periods of time. These facilities provide an ideal environment for the close study of the life history of chronic disease, the accurate evaluation of response to therapy, and the precise clinical, pathological, or chemical classification of disease.

The handicaps of research programs in the chronic disease hospitals include the serious limitation of personnel with time available for research and geographic and professional isolation. A possible solution might be found in the pooling of resources—the creation of a few specialized laboratories to which selected patients, or material from rare cases might be sent for study.

Training grants in neurosurgery inaugurated by NINDB

Departments of neurosurgery now are eligible for training grants under NINDB's grants and awards programs. The postdoctoral grants in neurosurgery, initiated this year, are awarded to qualified neurosurgical centers. These programs are designed to provide research training for individuals in preparation for careers in teaching and research. They will provide support for neurosurgical training on the same basis and under the same policies adopted for all other neurological and sensory disciplines and specialties.

New teacher-investigator training grant program established

Institutions that do not have full-scale training programs can take advantage of a new NINDB program of teacher-investigator training grants for all areas of research related to neurology.

The first award under the program was made to Dr. Philip P. Ellis, University of Colorado, for work in opthalmology. Other applications are under consideration in areas ranging from neurophysiology to neurosurgery.

These awards are intended to add a full-time staff member to institutions who will serve as a focus for neurological research and teaching in his department. Titles under which these persons will work will be left to the discretion of the individual institutions.

Proceedings of conference on hearing published

A published monograph entitled "Neural Mechanisms of the Auditory and Vestibular Systems," has resulted from an earlier NINDB-sponsored conference at Bethesda.

Among the specific topics discussed in detail are electron micrographic studies, histopathologic studies and role of the cochlea, anatomy, and physiology of the auditory cortex, studies with implanted electrodes, and afferent and efferent auditory connections.

The book is edited by Dr. Grant L. Rasmussen and William F. Windle, NINDB staff members, and is published by Charles C. Thomas.

New brochures on cerebral palsy and mongolism published

A new booklet titled "Cerebral Palsy—Hope Through Research," published this year, explains in laymen's terms the nature of cerebral palsy and related problems, and suggests where help may be sought. Research at NINDB and other institutions is described as the basis of hope for discovery of preventives and improved treatments. This leaflet is listed as PHS publication No. 713, Health Information Series No. 95.

"Mongolism—Hope Through Research" is another brochure for laymen printed this year. Research in all problems of mental retardation at NINDB and other research centers is described. Because of demands from States with Spanish-speaking populations, the booklet was translated and published in Spanish. The leaflet, which has a selected list of references, is listed at PHS publication No. 720, Health Information Series No. 94.

Both brochures are available on request from NINDB or from the Government Printing Office.

NATIONAL CANCER INSTITUTE

WITNESSES

DR. KENNETH M. ENDICOTT, DIRECTOR, NATIONAL CANCER INSTITUTE
DR. DAVID E. PRICE, DEPUTY DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
PUBLIC HEALTH SERVICE			
11 Personnel compensation:			
Permanent positions	6,696	8,480	8,525
Positions other than permanent	354	332	332
Other personnel compensation	135	103	103
Total personnel compensation	7,185	8,915	8,960
12 Personnel benefits	431	523	540
21 Travel and transportation of persons	356	412	420
22 Transportation of things	56	54	50
23 Rent, communications, and utilities	147	170	170
24 Printing and reproduction	166	213	220
25 Other services	21,089	24,039	23,449
Payment to—			
"National Institutes of Health management fund"	6,092	6,828	7,625
"Bureau of State Services management fund"	27	27	41
26 Supplies and materials	1,205	1,261	1,303
31 Equipment	326	417	401
41 Grants, subsidies and contributions	47,112	65,977	65,366
Subtotal	84,192	108,835	108,545
Deduct quarters and subsistence charges	20	20	20
Total, Public Health Service	84,172	108,815	108,525
ALLOCATIONS TO VETERANS' ADMINISTRATION			
11 Personnel compensation:			
Permanent positions	391	504	504
Positions other than permanent	90	70	70
Other personnel compensation	4	3	3
Total personnel compensation	485	577	577
12 Personnel benefits	31	36	36
21 Travel and transportation of persons	58	42	42
22 Transportation of things	1	1	1
23 Rent, communications, and utilities		1	1
24 Printing and reproduction	1	1	1
25 Other services	15	12	12
26 Supplies and materials	21	23	23
31 Equipment	65	75	75
Total, Veterans' Administration	676	768	768
Total obligations	84,848	109,583	109,292

Personnel summary

	1960 actual	1961 estimate	1962 estimate
PUBLIC HEALTH SERVICE			
Total number of permanent positions	1, 261	1, 351	1, 365
Full-time equivalent of other positions	59	51	51
Average number of all employees	1, 169	1, 235	1, 356
Number of employees at end of year	1, 255	1, 304	1, 315
Average GS grade	6. 0	6. 3	6. 3
Average GS salary	$5, 315	$5, 850	$5, 834
ALLOCATION TO VETERANS' ADMINISTRATION			
Total number of permanent positions	85	93	93
Full-time equivalent of other positions	10	8	8
Average number of all employees	85	90	90
Number of employees at end of year	90	102	109
Average GS grade	6. 0	5. 7	5. 6
Average GS salary	$5, 405	$5, 571	$5, 439

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(a) Research	34, 617	51, 522	50, 411
(b) Fellowships	2, 205	2, 400	2, 400
(c) Training	6, 855	7, 055	7, 055
(d) State control programs	2, 190	3, 500	3, 500
(e) Community demonstration projects	1, 347	1, 500	2, 000
Total, grants	47, 214	65, 977	65, 366
2. Direct operations:			
(a) Research	11, 454	14, 167	14, 347
(b) Review and approval of grants	910	1, 233	1, 247
(c) Professional and technical assistance	4, 685	6, 054	6, 174
(d) Chemotherapy contracts	19, 735	21, 643	21, 538
(e) Administration	415	552	620
Total, direct operations	37, 199	43, 649	43, 926
Total program costs	84, 414	109, 626	109, 292
3. Relation of costs to obligations:			
Costs financed from obligations of other years, net (—)	--------------	−43	--------------
Obligations incurred for costs of other years, net	434	--------------	--------------
Total obligations	84, 848	109, 583	109, 292
Financing:			
Comparative transfers to other accounts	183	220	--------------
Unobligated balance lapsing	6, 227	1, 197	--------------
New obligational authority (appropriation)	91, 257	111, 000	109, 292

GENERAL STATEMENT

Mr. FOGARTY. Dr. Endicott, are you ready to proceed?

Dr. ENDICOTT. Mr. Chairman, I have a prepared statement which I suggest we supply for the record, and I will summarize it briefly.

Mr. FOGARTY. All right, go ahead, Doctor.

(The statement follows:)

Statement by Director, National Cancer Institute, Public Health Service

Mr. Chairman and members of the committee, it is a great pleasure to appear before this body as Director of the National Cancer Institute. Over the past several years I have had the opportunity to testify on various programs of the National Institutes of Health, but never before in this capacity. During these first few months I have been engaged in a reorganization of the Institute in order better to face the future and to pursue with vigor several fresh and definitely promising approaches to cancer research which have emerged out of all our work in past years so liberally supported by the Congress. Before discussing the future course of our activities, however, I should like to comment on some of the pertinent research accomplishments and program developments of the past year which form an important part of the base from which new concepts have been evolved and new studies designed.

EXAMPLES OF RECENT RESEARCH FINDINGS

Differences by sex in survival

I would mention first some highlights of significant findings from a continuing study of end results in the treatment of cancer that is probably the most extensive of its kind ever undertaken.

The Cancer Chemotherapy National Service Center is compiling data received annually from 10 individual hospitals and the cancer registries of the States of California, Connecticut, and Massachusetts, and the Veterans' Administration. To date, they have gathered information about 300,000 patients.

A study of the survival experience of cancer patients in 99 hospitals throughout the country showed that in the last 10 years 62 percent of 116 women survived 5 years after surgery for localized lung cancer, compared to only 30 percent of 650 men. Significant differences favoring women were also found for cancer of the thyroid gland, tongue, and salivary gland, for skin melanoma, and Hodgkin's disease. The study also indicated that since 1951 there has been an improvement in survival for patients of both sexes with cancer of the large intestine, rectum, and thyroid, and for women with cancer of the uterine cervix and corpus.

The purpose of this program is to facilitate meaningful evaluation of end results in cancer, and particularly to compare the results of surgery and radiation with those of chemotherapy.

Combined therapy in breast cancer

It will be noted that the study described above makes no mention of improvement in survival for women with breast cancer, which remains the leading cause of death from malignant disease in that sex. This gives special importance to the preliminary results of research done by a group of National Cancer Institute grantees on treating breast cancer by combined surgery and chemotherapy.

In this study 107 women considered good candidates for curative surgery underwent radical mastectomy. Fifty-seven of them received the anticancer drug, thio-TEPA, administered intravenously on the day of the operation and the next 2 days. The remaining 50 patients received no drug.

Half of the women who received no drug developed recurrences within 2 years while less than one-fifth of those who received thio-TEPA had reappearance of disease.

Although these results are preliminary and their true significance will depend on additional data gathered over a longer period, the study offers the hope that adjuvant chemotherapy may markedly increase the benefits of surgery for breast cancer.

This study and others like it that are now in progress or being planned are of great importance, not only because they may lead to substantial improvement in methods of treating breast cancer, but for several other reasons as well. Let me mention two of them. Chemotherapy is being attempted with these patients much earlier in the course of their disease than is usually the case.

Ordinarily, drugs are given to cancer patients when every other possibility of more conventional treatment has been exhausted; in other words, when the disease is advanced, or widespread. But the study I have just described would seem to suggest that the earlier anticancer drugs are employed, the greater may be their therapeutic effect.

It should be emphasized, however, that such research is only just beginning and that for every success we must expect many failures. In this connection I regret to report that studies on the combined use of drugs and surgery in cancer of the lung, stomach, and large bowel have shown nothing encouraging—at least with the drugs selected for the first studies.

This discovery, if it holds up, will be of great significance in itself. Almost as important, however, is the increased attention it focuses on (1) the desirability of a renewed effort on surgical adjuvant studies, (2) the fact that the potential of some of the older drugs has not yet been realized because of research yet to be done, and (3) that failure of combined surgery and drug therapy in one type of cancer does not mean this will be true of all types of cancer.

Clinical research in leukemia

National Cancer Institute scientists, in collaboration with those of other Institutes at NIH, have produced a number of findings in the past couple of years that are important to the management of hemorrhage, a principal cause of death in leukemia patients.

These studies at the clinical center have shown that fresh blood is more effective in preventing spontaneous bleeding than is blood kept for a time in the blood bank. Getting fresh blood, however, is often a serious problem, particularly in an emergency situation. In a study which is still in progress, but from which satisfactory results have already been obtained, National Cancer Institute and Division of Biologics Standards investigators are collaborating on a new method of processing blood.

By this method it is possible to get platelet-rich plasma from the blood, which is highly effective in arresting hemorrhage. Not only this, but the red cells of the blood can be returned to the donor, thus enabling him to give blood more often. This is full of meaning, of course, to the parents of leukemic children, who are anxious to make frequent blood donations as a means of giving practical help to the patient.

Chemotherapy of Choriocarcinoma

I am able to report encouraging progress in the National Cancer Institute's study of the chemotherapy of uterine choriocarcinoma, a highly malignant tumor which develops from the pacenta during pregnancy. To summarize this important work briefly, for the past several years scientists of our Endocrinology Branch have been treating this disease by giving massive doses of methotrexate, a drug commonly used against acute leukemia. In all, 63 women with choriocarcinoma have been treated at the clinical center. Thirty of them have responded in a most dramatic fashion. All traces of their disease have vanished, and they have remained apparently free of cancer for periods ranging from 3 months to more than 5 years. Twenty-five patients experienced incomplete remission and subsequently died, and one patient has shown no response whatever to the treatment. Seven are still undergoing therapy.

We cannot be other than enthusiastic about the results of this study. Nearly every one of these patients was afflicted with far advanced disease at the time the drug treatment was begun, and some were near death. Their malignancy had extensively invaded the pelvic region and metastasized to the lungs and brain. Yet, half of these women are now in what appears to be perfect health. It is impossible to state with assurance that their disease has been permanently eradicated, but this study shows how chemotherapy can produce long-term remission in patients beyond help by any other known form of treatment.

Effects of cigarette smoke on lung tissue

Numerous studies have implicated cigarette smoking as a causative factor in the increasing incidence of lung cancer. Recently, the manner in which cigarette smoking may play a role in the development of lung cancer was observed by scientists working partly under grants from the National Cancer Institute and the Division of General Medical Sciences.

Segments of tissue that line the respiratory tract were exposed to cigarette smoke products in a specially designed chamber. Mucus production was seen to increase sharply within a few seconds after smoke was introduced. Then for about 16 minutes, the flow decreased. Finally, there was a 30-minute recovery period in which the flow returned to normal. When the segments were exposed repeatedly to smoke products, as in typical smoking conditions, the inhibitory effect was greatly intensified.

The scientists conclude that smoke impedes the normal cleaning action of the lining of the lungs, thus permitting particles in the smoke to penetrate the tissue and cause irritation which might lead to cancer. They add that the effect is a physical one and could be produced by numerous other environmental irritants.

Leukemia virus in mice and rats

A year ago, Dr. Heller reported to this committee that Dr. John B. Moloney, of the Laboratory of Biology, had isolated a virus which produces leukemia in mice of several strains and in adult as well as newborn animals. This type of leukemia is virtually undistinguishable from the spontaneous form of the disease in mice. Dr. Moloney has since shown that rats, too, are susceptible to the virus.

Perhaps the most interesting new information about this virus is a finding that it can be transmitted in mice from a mother to her offspring through the placenta. This mode of transmission was demonstrated in a collaborative study by Dr. Moloney and Dr. Noriaki Ida at the M. D. Anderson Hospital and Tumor Institute, Houston, Tex. This finding suggests the possibility of mother-to-offspring transmission of naturally occurring leukemia.

The foregoing are but a few examples of the significant results that are being obtained from research on cancer. I should like to go on now with a review of progress made during the year in our programs as a whole, and explain how our planning for the future is guided along the directions in which past accomplishments have been taking us.

CHEMOTHERAPY PROGRAM

The activities of the Cancer Chemotherapy National Service Center are proceeding, for the most part, smoothly and productively. Many groups, including public and private research institutions, the pharmaceutical and chemical industries, universities, medical schools, and several agencies of Government are collaborating effectively in the search for useful anticancer drugs and methods of employing them. I want to commend the staff of the service center in particular for the manner in which it has coordinated so many diverse research and development operations and forged them into a highly efficient tool for progress in cancer chemotherapy.

I have had a report prepared which goes more fully into major facets of this program, in case the committee should wish to have more detailed information. We have recently viewed the entire program supported under grants and contracts, and have made many internal adjustments to make the best use of funds available. We have increased our investment in preclinical workup for active drugs and reduced support of screening and related activities which are designed to disclose new drugs. This has been done to compensate for increased costs of research and testing in the current market and to support preclinical pharmacology and other work designed to ready the greater volume of active compounds for trial in man.

At another time we may increase our investment in clinical trials financed under grants, and reduce our contract program. Such shifts in emphasis are necessary in drug development programs, but must be done with great care because research and testing teams cannot be assembled and trained as readily as one would wish. So far, we believe adjustments made in the programs have been accomplished with only minor disruption to those activities which must be continued, although at a lower level.

VIRUS RESEARCH

During the year, a good deal of effort has been devoted to planning the basic requirements of a long-range and broadly supported program of research on viruses in relation to cancer. National Cancer Institute grant support of this work totaled more than $5 million in calendar 1960, and the increased activity in this area has produced heavy demands for vital research materials.

The most urgent need was for standard cultures of animal and human tissue cells essential for the study of viruses. This need is being met in part through a committee established to develop criteria for certifying and preserving strains of mammalian cells of interest in cancer research. Well over a dozen laboratories throughout the country are interested in assisting with this effort, and the American-type culture collection here in Washington will serve as a repository and distributing center for standard cell strains.

To fill another need of cancer virologists, the National Cancer Institute awarded a contract to the University of Kansas Medical Center to develop diagnostic reagents which will identify known viruses of the human digestive tract. It is interesting to note that in this instance we were able to take advantage of laboratory resources previously developed by the National Foundation in their search for a polio vaccine.

These are some of the service needs which must be met to assure progress in the virus-cancer field. Much more must be done to realize the potential that leading scientists believe this field offers.

The National Advisory Cancer Council has recommended that the National Cancer Institute undertake a coordinated virus program somewhat similar to that developed in chemotherapy. The Council recommends that both grant and contract mechanisms be applied to accomplish the following: (1) Collection, preservation, and distribution of human cancer tissue for virus studies; (2) development and procurement of typing reagents for animal viruses, with independent confirmation as needed; (3) production of adequate quantities of typing reagents for all known viruses for which the production protocols are fully developed, with arrangements, when necessary, for independent confirmation, standardization, and certification of viral typing reagents: and (4) design and encouragement of the production of liquid nitrogen refrigerators for individual laboratory use to permit long-term preservation of mammalian cells, tissues, and other necessary biological reagents.

The Institute has also been urged to take the lead in developing experimental animals whose viral and genetic components are known, along with special facilities for housing these animals in a manner which will prevent viral contamination. Such animals are just as essential to the biologist in virus research as a compound of known purity is to a chemist. The National Cancer Institute plans to work closely with interested groups in other Institutes to encourage a cooperative program of viral investigation in the primate stations currently planned and financed by the National Heart Institute, and to determine what must be done to make primates available for research in the virus-cancer field.

Finally, the Advisory Council has recommended that the National Cancer Institute establish two or more regional centers, in west and east coast areas, for summer training of experienced investigators in the virus-cancer field.

All of this will be implemented as rapidly as possible.

FIELD STUDIES AND DIAGNOSTIC RESEARCH

The results of laboratory and field studies in carcinogenesis conducted over a long period of years have convinced us that there is much to be gained by accentuating and expanding our studies of cancer in human and animal populations. Indications are that important cancer-causing factors can be thus defined which will greatly increase the efficacy of preventive methods based on epidemiological findings. This approach has already been rewarded in the establishment of an impressive number of industrial carcinogenic situations, and of the role of tobacco smoking in lung cancer.

Longtime observation of uranium miners, for instance, has given indications of an increased risk to lung cancer in this occupation, and this has stimulated public health activity toward reducing the hazards. More research is needed on this problem, of course, but preventive measures are always in order where a hazard seems to exist.

The future course of laboratory and field research on cancer in the population will most certainly have to take two definite directions. One is toward the elucidation of specific factors, either by studying groups exposed to heavy concentrations of suspected carcinogens, or by retrospective case-control analyses of specific types of cancer. The other is the study of large population groups and their environments, the so-called "human population laboratories." This constitutes an area of research—both laboratory and field—which I consider to hold the promise of early, practical results.

Another interesting aspect of this kind of study is that we have become increasingly aware of the widespread occurrence of cancer in animals in their natural environment. This suggests the possibility that some animal cancers may be related in some way to cancer in man. Although there is no scientific evidence that cancers are transmitted from animals to man, the disease in man and animals may very well be a reaction to the same environmental or infectious agents.

Leukemia and related cancers, for instance, are among the primary causes of death in pullets and hens, presenting an economic problem long recognized and studied by the Department of Agriculture. Leukemia is also seen in cattle, and presents an economic problem in Denmark and Germany. Cancer of the bladder is frequently found in cattle in some parts of Turkey and Africa. In fact, domestic animals develop a wide variety of cancers. We now have evidence also that wild mice, which inhabit our granaries, may carry and liberate the polyoma virus which causes a wide variety of tumors in mice, rats, and hamsters.

Undoubtedly the most perplexing problem of this nature to develop recently occurred late last year in the discovery that rainbow trout in this country have a high frequency of liver tumors. This is a situation with both health and economic implications. Studies are progressing to clarify the cause of the disease, and the best possibility seems to lie in the analysis of some new types of pellet diets on which most of the trout are now raised.

So important do we consider the need for intensified study of the occurrence of cancers in animals, and their possible relationship to cancer in man, that a program in cancer epizoology is being developed by the National Cancer Institute. The entire new approach to field studies is considered of great importance and will be pursued insofar as feasible.

Research on cancer diagnosis has been centered in a Diagnostic Research Branch and integrated into our general area of field studies.

These studies have thus far produced a useful public health tool in the cell examination test for uterine cancer, a major program objective of cancer control as I will explain later. Most of this research has been completed and our attention shifted elsewhere. Research has been continued on exfoliative cytology as applied to detection of cancer of the lung, stomach, lower intestinal tract and urinary tract. In this work the most promising lead appears to be examination of the urine for bladder cancer cells.

The diagnostic program also includes investigation of a wide variety of biochemical procedures for their possible utility from three standpoints: (1) as aids in the differential diagnosis of actual cancer patients, including the possible prognostic value of abnormalities or changes that may be detected; (2) as screening procedures that may aid in the detection of unrecognized cancer in people without symptoms; and (3) as possible means of distinguishing characteristics of people that may be associated eventually with the development of cancer.

This third aim is closely associated with epidemiology, and involves long-term follow-up of people on whom the tests would be performed. This might run into such a sizable operation as to require the use of electronic computers in the statistical processing of data.

The current scientific concensus is that a universal cancer test is no more likely to be found than a single cause of cancer. Our diagnostic research is therefore oriented along the narrow lines of specific cancer entities. This is a long-range, painstaking procedure which will probably produce a long series of slow gains rather than a sudden breakthrough.

CONTROL PROGRAM

The cancer control program, which receives technical guidance from the Director of the National Cancer Institute, is located in the Bureau of States Services. The program's unique contribution to the fight against cancer lies in its efforts to help reduce the lag between the confirmation of new methods of controlling or preventing cancer and the application of these methods as quickly and as competently as possible in communities throughout the country. The cancer control program's efforts have been strengthened by the addition of community cancer demonstration project grants and by increases in assistance for State control programs.

The community demonstration project grant program was designed to stimulate the wider use of new and confirmed practices, as defined by local conditions and needs. By aiding projects that unify community health agencies in an attack upon particular causes of cancer, the "payoff" on validated control techniques is hastened, and benefits are realized on the widest possible basis. Recognizing that diverse talents and specialties are requisite to the success of demonstration projects, the cancer control program and its advisory committee have encouraged sponsors of projects to involve all the interested medical and allied groups in their communities. The projects that have been selected for grants have been carefully scrutinized by appropriate State health officers and by the advisory committee to the cancer control program, which is composed of 14 non-Federal medical consultants with broad and diversified experience in cancer control.

Special priority has been assigned by the cancer control program and its advisory committee to stimulating early casefinding of uterine cancer. Although proper use of the Papanicolaou smear, in conjunction with tissue-study and pelvic examination, could virtually eliminate uterine cancer as a cause of death, 15,000 women a year are dying from this disease. A four-pronged attack on uterine cancer has therefore occurred: (1) grants to agencies that examine women in low-income groups where uterine cancer is most prevalent; (2) support for educational activities that will increase the cytodiagnostic skills of family physicians, technicians, and others; (3) assistance for evaluating public educational services; (4) aid to the development of laboratory services. The 67 demonstration project grants approved to date give evidence of the significant contribution this new approach can make; agencies and resources working to control uterine cancer are being increased in communities throughout the country.

In 1961, for the first time in more than a decade, grants to support State cancer control programs were enlarged. The formula for allocating these funds has been adjusted so that a minimum of $25,000 is available to each State, which will support a basic control program. With these additional funds, some State health agencies have expanded their casefinding activities in order to diagnose cancer at early and treatable stages, and some have added to their clincal, nursing, and followup services to improve the care of patients.

In addition to the efforts entailed by the demonstration and formula grants, the specially trained members of the cancer control program have assisted, through consultation, in the development and conduct of statewide programs and local projects. They have published a directory of cancer control services, facilities, and programs in all the States. They have developed educational programs with national professional organizations concerning advances in cytodiagnosis and along lines suggested by the evidence which associates smoking with lung cancer. And they have undertaken other cooperative activities with professional and voluntary agencies to take maximum advantage of current knowledge in the control of cancer.

REORIENTATION OF NEW APPROACHES

As I intimated in the introductory portion of this statement, we have arrived at a point in the whole development of cancer research and related endeavors where new and well-defined avenues of approach to cancer problems have opened up. In order to take advantage of these opportunities and throw our resources into proper gear for a renewed effort, we have undertaken a reorganization of the National Cancer Institute in which our operations have been regrouped around these new approaches.

All of our research grants and training activities have been consolidated under an Associate Director and will be administered through several different branches. Field investigations, including those dealing with the ecological factors in cancer research and with diagnostic tests, will be similarly administered under another Associate Director. The Chief of the Cancer Chemotherapy National Service Center has also been designated an Associate Director for administration of those activities.

The clinical center concept

The clinical center concept as a means of seeking the optimum results from an integrated, multidisciplined approach to medical research problems, has several facets of both scientific and practical appeal which make it a logical and even compelling development in the evolution of cancer research.

I need not go over again the ground covered by Dr. Shannon concerning the clinical center concept as a whole, but I would like to comment on the need for pursuing this kind of opportunity in the area of cancer. Several of the top staff members of the National Cancer Institute accompanied me recently on visits to selected institutions where we discussed the opportunities, special problems, and other aspects of their prospective participation in cancer center programs. One of the most interesting revelations to us was to see how much has been accomplished in clinical research with the meager resources available to these institutions. For instance, at one of the leading chemotherapy research centers in the South, the principal investigator does not have a single research bed. Studies in patients must be carried out in the busy wards of a county hospital, while laboratory work is done on the second floor of an old warehouse some distance away, and the work with animals in the embalming room of an old funeral parlor. Another prominent cancer institute in the South was built a few years before the modern concept of the need for extensive laboratory facilities to underpin a clinical program. There we saw a magnificent hospital well equipped with basic laboratories. However, the staff cannot make full utilization of the cancer beds until every floor is equipped with additional laboratory space and facilities for clinical work. We believe that the cancer program in support of centers, if properly carried out, will accelerate research in a wide variety of situations.

The National Cancer Institute is cooperating with five other Institutes contributing equal shares from our fiscal 1961 appropriations to a $3 million program for the planning, negotiating, and initial support of clinical research centers spanning the interests of these Institutes, namely cancer, arthritis, allergy, heart, mental health, and neurology investigations.

Grants for construction

The National Cancer Institute is engaged now in administering the granting of $5 million in nonmatching construction funds for cancer research facilities which was included in our 1961 appropriation. This program, which was authorized for 1 year, will enable a number of institutions having good cancer research programs to provide themselves with buildings and equipment needed for their development of research activities.

Applications for these construction grants were required to be filed by January 15, and will go before the spring meeting of the National Advisory Cancer Council for consideration and recommendation. We are processing these applications the same as research grant applications, including review by staff members and consultants, and project site visits where necessary. To be eligible for a grant, an institution must be actively engaged in cancer research of high quality. It must also show that construction is clearly needed for more effective cancer research by the key scientific staff already employed, that the amount needed is substantial when measured against available and potential resources, that every effort has been made without succeess to secure matching funds, and that the cost of the proposed construction is reasonable.

Other integral programs

I have already discussed our chemotherapy and field studies activities in terms of planning for future operations along the principal new approaches to cancer problems. In addition to these and support of clinical research centers, there are other important programs in which the National Cancer Institute is participating, as are other Institutes and Divisions of the National Institutes of Health.

One of these has to do with exploiting the resources, both in scientific manpower and fields of study, that are available in other countries. The Institute is already supporting a program presently administered through the National Institute of Allergy and Infectious Diseases, for the establishment of research centers abroad which will be tied in with American universities having grant-supported research programs. These will be set up chiefly to take advantage of situations in foreign lands which present good medical research opportunities, and with the closest collaboration between the American institution and the foreign center. It is our hope that in the field of cancer we can look to the esablishment of programs to study epidemiological and other factors of malignant disease among populations in Africa and South America. There are excellent possibilities in such programs on which we are eager to capitalize.

Program adjustments

Throughout this statement there have been references to reorganization and reorientation affecting our various programs. This procedure, designed to take advantage of the opportunities offered by new approaches to cancer problems, involves some adjustments in certain activities. For example, within the program of the Cancer Chemotherapy National Service Center, a total of $1.3 million in grant funds for clinical trials has been shifted to contracts in order to maintain balance and to achieve maximum utilization of available funds. As already noted, we will concentrate less on preliminary screening of untried compounds in order to step up the pharmacological processing of promising materials and get them into clinical trial and hopefully into the hands of physicians for the benefit of cancer patients.

New cancer building planned

One of our most urgent problems has to do with space in which to house research and related Institute activities at Bethesda. A study of our program plans in relation to space requirements is proceeding as authorized and appropriated for in our 1961 budget. We are planning a new laboratory-office building to be erected at the National Institutes of Health which will contain approximately 128,000 square feet of floorspace and permit expansion and consolidation of the intramural and extramural components of the Institute's research program. We are grateful to the Congress for its action last year, for this building will enable us to carry out our new programs which would otherwise operate under severe handicaps and in some cases could not be done at all. Next year we will be requesting funds for construction.

CONCLUSION

In conclusion, Mr. Chairman, the revised request for 1962 is $117,167,000, as compared with the adjusted 1961 appropriation of $110,980,000. This allowance, although containing a $5 million decrease for nonmatching construction grants provides additional funds in a number of activities.

The largest of these are:

(1) An increase of $8,683,000 in research grants will permit us to pay a larger proportion of approved grants. Approximately $2 million of these funds will be used for programed grants in chemotherapy. Also included in this increase is $2 million for large grants such as those for cancer centers.

(2) An increase of $500,000 for additional community demonstration projects in cancer control—an important step in bringing the benefits of research to the people.

(3) An increase of $526,000 for direct research which will permit us to intensify studies in our laboratories and with patients in the clinical center. We are particularly interested in pushing ahead with leukemia and biology studies, in developing techniques for using automation and mathematics in the solution of clinical and laboratory problems and with the exploitation of challenging leads in virology.

(4) An increase of $2,300,000 for virus and chemotherapy contracts and related service activities. These funds will permit the virology program to move rapidly forward by providing services to individual scientists in accordance with the Council and staff rceommendations discussed above. In chemotherapy additional contract funs will permit us to ready more compounds for the clinical trials which will be expanded using additional research grant funds. Other smaller but no less important increases are described in the budget document.

Grants:	
Research	$55,205,000
Fellowships	2,400,000
Training	7,055,000
State control programs	3,500,000
Community demonstration projects	2,000,000
Subtotal, grants	70,160,000
Direct operations:	
Research	14,777,000
Review and approval of grants	1,400,000
Professional and technical assistance	7,631,000
Chemotherapy contracts	22,538,000
Administration	661,000
Subtotal, direct operations	47,007,000
Total 1962 appropriation requested	117,167,000

Dr. ENDICOTT. As you know, I am new in this job. Last year I was——

Mr. FOGARTY. You have been there almost a year, haven't you?

Dr. ENDICOTT. About 8 months, sir.

Mr. FOGARTY. Well that is about three-quarters of a year. You knew a lot about the Cancer Institute before you took this job, didn't you?

Dr. ENDICOTT. A little.

Mr. FOGARTY. Go ahead.

Dr. ENDICOTT. It has been a very unusual year for the Institute because it has been a year of rather great change in the entire management of the Institute.

As you know, Dr. Heller left, and Dr. Mider, our Scientific Director, left at the same time. And on top of this somewhat difficult change in the entire top management of the Institute, we also were confronted with several very important new programs.

And, as a matter of fact, I think this is a real milestone year for the Cancer Institute in that our budget is equivalent to the size of the National Institutes of Health budget the year Dr. Shannon became Director.

THE CHEMOTHERAPY PROGRAM

This seemed a splendid opportunity, since we did have so many changes, to undertake a very searching reexamination of our present posture and of the big problems ahead of the organization, staffing and so on, that would be required for the future. Now these studies of the organization, fortunately, were started during the previous year, and I have had an opportunity to discuss for some time with Dr. Heller the major changes which appeared to be necessary. And we have spent the past 8 months in a continuing, searching study of what seemed to be wrong with our organization and what might be done about it.

I might mention some of the key problems. We manage an altogether unique drug-development program. This cancer chemotherapy program is certainly the largest drug-development program in the history of the world.

Mr. FOGARTY. You are very familiar with the chemotherapy program?

Dr. ENDICOTT. Yes, sir; and I am very pleased to report that Dr. Sessoms improved it a great deal since I left it.

In this area a study has been going forward for about a year. The final reports become available during the fall.

TRANSFERS OF FUNDS FROM GRANTS TO CONTRACTS

We have made substantial rearrangements within this program which necessitated the transfer of some funds from the grant area to the contract area. This transfer has been carried out. It is not reflected in the budget presentation as those figures were not available at that time.

The chemotherapy program is now, I think——

Mr. FOGARTY. You better give us a pretty good explanation of these transfers for the record if it is not in your justification.

(The explanation requested follows:)

EXPLANATION OF TRANSFER OF FUNDS FROM GRANTS TO CONTRACTS, CANCER CHEMOTHERAPY PROGRAM

Within the total of the 1961 appropriation "National Cancer Institute" $1,300,000 has been transferred from "Research projects" to "Chemotherapy contracts." This action was taken subsequent to a program review by the staff of the Cancer Chemotherapy National Service Center with the advice of the Chemotherapy Review Board of the National Advisory Cancer Council. The review identified areas requiring changes in emphasis in order to maintain proper balance in the work which is resulting in a progressively increasing number of active antitumor agents. Some of the necessary financial adjustments were made through the reduction of some contracts and the elimination of others. These adjustments, together with the transfer, were required in order to accomplish the goals established for 1961.

The funds under "Research projects" support grants for the clinical evaluation of chemotherapeutic agents. In the stage of development where preclinical work on drugs had become backlogged, it was believed more expedient to support additional contracts even though this would necessitate some reduction in the support for clinical studies. These contracts are essential to the orderly progress of the work underway and are organized to expand efforts in the secondary evaluation of compounds which have passed the criteria for active agents, to expand the spectrum of animal test systems for antitumor agents, and to prepare the increasing number of active compounds for clinical evaluation.

The contract proposals that have been designed to meet these program needs have been submitted at the request of the staff of the Cancer Chemotherapy National Service Center and will be integral parts of the centrally planned program. It is necessary to contract for these activities in order that the terms be carried out strictly as specified under the direct supervision of the center staff. This proposal has the approval of the National Advisory Cancer Council.

The proposal to effect this transfer of funds was submitted to the chairmen of the Labor-HEW Subcommittees of the Committees on Appropriations during December 1960.

SPECIAL REPORT ON CHEMOTHERAPY

Dr. ENDICOTT. Yes, sir. There is a special report on the chemotherapy program which I would be happy to supply for the record.

(The report referred to follows:)

CANCER CHEMOTHERAPY PROGRAM

The drug research and development program of the Cancer Chemotherapy National Service Center, National Cancer Institute, has substantially accelerated the flow of potential anticancer drugs into clinical trials during the past year. In addition, notable progress has been made in the endocrinology program, from which 10 percent of the hormonal substances studied are found to be clinically interesting. An important factor contributing to this high level is the cooperation of industry, which participated through contractual arrangements for preparation of steroids. This brief report summarizes the status of the Chemotherapy Service Center's program activities for fiscal year 1961. Indications of probable future trends are discussed.

HISTORY

The National Cancer Institute took initial steps leading to the development of a concerted chemotherapy program in 1953 when, acting on the recommendation of the Congress, it provided funds for the support of grants valued at $1 million to a group of institutions for research on the chemotherapy of childhood acute leukemia. The following year, funds for support of these grants were increased to $3 million. In the meantime, plans were being made for the establishment of an engineered drug-development program such as exists today. The Cancer Chemotherapy National Service Center was organized in April 1955 to coordinate and accelerate anticancer drug research throughout the country by making available services (such as screening), technical information, and funds to support promising and necessary investigations.

The center was created under joint sponsorship of the National Cancer Institute, Food and Drug Administration, Veterans' Administraton, Atomic Energy Commission, American Cancer Society, and Damon Runyon Memorial Fund for Cancer Research. During its nearly 6 full years of existence, virtually all funds for the service center's program have been incorporated in the annual appropriation to the National Cancer Institute. During the present fiscal year (1961), approximately $28 million is allocated to the chemotherapy program, about $21.5 million of which is earmarked for contracts. Nearly $5.3 million is allocated to pay for programed grants for clinical trials of anticancer agents. In addition, $11 million of regular grant funds have been used to support chemotherapy research not directly associated with the service center's program. This year, therefore, the National Cancer Institute will invest approximately $35 million in efforts to find, develop, and put into use effective anticancer drugs.

CURRENT STATUS

Drug procurement

A wide variety of materials is obtained by the service center for antitumor testing. They include synthetic chemicals, antibiotics, hormones and related compounds, extracts from plants and animal tissues, and others that do not fit into any of these categories. The materials are obtained in various ways: Many are donated free of charge by research institutions and industry; others are produced under contract by pharmaceutical and chemical firms, universities, and other institutions; and some are submitted by independent investigators. In all, more than 135,000 different materials have been received for anticancer screening since the inception of the program, and more than 540,000 separate tests have been done. The rate of procurement remains approximately 50,000 compounds per year.

Primary screening

The initial testing of these products for possible anticancer activity takes a variety of forms. Most materials are subjected to a screen consisting of three transplantable mouse tumors, originally chosen because of their ability to detect anticancer activity in agents already known to be effective against human cancer. A relatively small number of materials, submitted to the Chemotherapy Service Center in quantities insufficient for animal testing, are studied initially in tissue culture, which requires only minute amounts of material. Compounds showing activity are synthesized in larger amounts for study in mice. Hormonelike chemicals are assayed for biological activity in mice, on the assumption that materials possessing hormonal properties may reasonably be expected to affect the growth of human tumors such as cancer of the breast and prostate gland. In the aggregate, screening yields between 400 and 600 compounds per year that are of sufficient promise to merit further study.

The screening mechanism employed by the Chemotherapy Service Center is recognized as a compromise between the ideal and the practical. Ideally, a cancer chemotherapy screen would permit the selection of all effective agents submitted to it and no others. It would provide information on the degree of activity of each material, the specific form or forms of human cancer against which it would be active, and the undesirable, toxic side effects it would cause in man. It would, furthermore, rank agents in order of their effectiveness and in this way preclude unnecessary followup of second-rate agents. Such a screen does not exist and may be beyond the realm of possibility. However, it is feasible to approach this ideal. Recent advances in the technology and methology of anticancer screening, largely developed by institutions and companies participating in the program, are providing opportunities for improvement in the primary screen. More animal tumors are becoming available for screening purposes; the supply of laboratory animals, including mice, rats, hamsters, and guinea pigs, has been tremendously increased within the past several years. And, perhaps of primary importance, information is gradually being accumulated that will permit the formulation of screening procedures that more accurately predict the performance of drugs in the clinic. The Chemotherapy Service Center, with the assistance of its responsible advisory groups, is investigating paths toward improvement of the primary screen through the incorporation of additional tumors, and simplification of methods.

During the present fiscal year, it has been necessary to reduce somewhat the level of primary screening in order to maintain balance in the total chemotherapy program. Careful and detailed review of the program indicated that available funds from the 1961 budget could best be utilized if greater emphasis were placed on preclinical evaluation of drugs already selected by the primary screen. This adjustment, which has been made, will result in the screening of fewer new materials. At the same time, however, information will be accumulated more rapidly on the growing number of promising materials under study.

Preclinical testing

Once a material passes the primary screen, it is subjected to a much broader exploration. These experiments have several objectives: (1) To rank closely related materials, and new materials, in terms of their degree of anticancer activity. Several animal tumors are employed in these experiments; (2) to ascertain the breadth of activity of an agent by employing it against a wide variety of rodent tumors; (3) to indicate the specificity of an agent, such as its ability to affect established tumors, spontaneous tumors, induced tumors, or those that have acquired resistance to standard chemotherapeutic agents; and (4) to show the effects of an agent against human tumors growing in laboratory animals.

Another part of this activity now is being carried out by tissue culture methods, in which drugs are tested against either living cells or microbes. These techniques have been especially useful in the study of antibiotics, where it is necessary to separate from a crude mixture that may contain many thousands of chemicals the one that possesses anticancer activity. This work formerly took years to complete. Now it can be done in a few months.

The goal of secondary evaluation is to provide the clinician with as much information about a promising drug as possible. Therefore, the final step in preclinical testing involves administering the drug to a few patients who have been carefully selected for this purpose. Once these studies are completed, the material is prepared in dosage form, ready for clinical investigation.

The endocrinology program

This portion of the Chemotherapy Service Center's program which stands apart from the routine primary and secondary screening activity, became fully operative in 1957. Since then, approximately 900 materials have been received for study. Although this is a small fraction of the total volume of Cancer Chemotherapy National Service Center drug testing, the yield of clinically interesting materials coming through the endocrinology program is roughly 10 percent of those studied, compared with a rate of about one-tenth of 1 percent for the nonhormonal compounds.

A major factor contributing to the high degree of success of the endocinology program is the cooperation of industry. Through contractual arrangements, steroid preparatory laboratories have been established by a number of the Nation's largest pharmaceutical firms. These laboratories, with their unique facilities for the synthesis and development of steroids, make available to the Chemotherapy Service Center many new and interesting compounds whose chemical structure suggests probable antitumor activity. After preclinical evaluation of those deemed especially promising for clinical study, the prep labs are requested to supply quantities sufficient for study in the clinic. This mechanism is now functioning efficiently and productively.

Clinical activities

While most other parts of the chemotherapy program have achieved and are maintaining a steady, high level of activity, the rate at which drugs have reached the clinical trials phase has expanded tremendously within the past year. This is a natural result of the 5½ years of growth since the Cancer Chemotherapy National Service Center was established, for an intensive effort has been directed toward increasing the flow of new anticancer agents into the clinic. Twelve months ago, 109 agents had been placed in clinical trial; now the number is 160. Within the year, the number of patients who have participated in these studies has risen from about 8,000 to 16,500, and now includes some in studies being carried on in Western Europe.

A recently completed analysis of the clinical activity showed that of the 160 agents currently under investigation, only 31 were being studied in the clinic prior to the inception of the Cancer Chemotherapy National Service Center program. The drugs that have been, or are being, evaluated are about equally divided between hormones and nonhormones.

In addition to the obvious gains to be made from clinical chemotherapy research, several other byproducts are worth mention. For instance, new statistical methods are being developed that permit agents to be studied initially in a small group of patients afflicted with different forms of malignant disease. In this way, clinicians can learn rapidly what type or types of cancer are most likely to respond to the administration of a new agent. Furthermore, the wealth of information stemming from the clinic is being fed back to investigators in the preclinical area, one of whose chief concerns is improving the correlation between screening and clinical results. Armed with vast amounts of data on clinical drug studies, those scientists who are working at the level of animal screening can redesign, augment, or otherwise modify their procedures so that their efforts will provide a better and more accurate prediction of a new agent's clinical value.

An especially noteworthy accomplishment of the Cancer Chemotherapy National Service Center clinical program, one that is referred to in the opening statement of the Director of the National Cancer Institute, is the observation that the anticancer drug, thio-TEPA, can substantially augment the benefits to be derived from surgery for breast cancer. In a group of patients who were treated by a combination of surgery and chemotherapy, the rate of recurrence of disease was dramatically reduced, in contrast to the results in patients treated only surgically. This finding will spearhead a major expansion in the so-called surgery adjuvant studies, for it provides the first clear evidence that chemotherapy may offer a means of greatly improving the therapeutic value of cancer surgery.

FUTURE TRENDS

The program of the Cancer Chemotherapy National Service Center is stable, but flexible. Despite a modest cutback in primary screening, new materials are being introduced at a rate so high that the pipeline of drug development activities is full. Clinical research will continue to expand as clinicians initiate new studies of existing drugs and accept for trial new agents coming out of the preclinical activity. Contract support of research and development will expand appropriately.

The principal net gain will be in the intangible area of information—new knowledge of the treatment of cancer; of the action of drugs, not only on malignant cells, but on the whole patient; of the biochemistry of malignant disease and consequently, how the biochemical pattern may be altered. This fund of knowledge is growing. Ultimately it will reach a point at which scientists will be able to design and use drugs that will provide vastly effective, long-term control of human cancer. This is an important milestone toward the goal of chemotherapy research, the cure of cancer. The program of the Cancer Chemotherapy National Service Center is moving steadily toward that end point.

USEFUL DRUGS IN THE TREATMENT OF CANCER

About 20 drugs are temporarily effective in controlling the growth of certain forms of cancer, relieving pain, and prolonging life. Their usefulness is limited by the undesirable side effects they cause and by the development in many instances of drug resistance. Some of their principal uses are summarized below.

ALKYLATING AGENTS

Nitrogen mustard is rated the best drug for Hodgkin's disease, and is somewhat effective against other lymphomas, mycosis fungoides, lung and breast cancer, and choriocarcinoma.

Triethylene thiophosphoramide (thio-TEPA) is useful in Hodgkin's disease and cancer of the ovary, and has some activity in malignant melanoma, lung and breast cancer, and neuroblastoma.

Triethylene melamine (TEM) is useful in Hodgkin's disease, lymphocytic lymphosarcoma, and the chronic leukemias, and is somewhat effective against cancer of the lung and ovary.

Chlorambucil is the best drug for chronic lymphocytic leukemia, lymphocytic lymphosarcoma, and giant follicular lymphoblastoma, and is useful in cancer of the ovary and moderately active in reticulum cell sarcoma.

Myleran is the best drug for chronic myelocytic leukemia.

Sarcolysin has been reported to be active in seminoma, a testicular tumor.

ANTIMETABOLITES

Methotrexate has produced complete remissions of uterine choriocarcinoma for as long as 5 years. It is useful in acute lymphocytic leukemia in children, and somewhat effective in reticulum cell sarcoma and lymphocytic lymphosarcoma.

6-Mercaptopurine is standard therapy for the acute leukemias, and is active against chronic myelocytic leukemia.

5-Fluorouracil has shown activity in cancer of the colon and bladder and in breast cancer in women.

HORMONES

Hormones, such as cortisone, hydrocortisone, prednisone, prednisolone, and ACTH, act quickly in a high percentage of children with acute leukemia. Therefore, therapy is usually initiated with one or more of these hormones, and continued until resistance to the drug occurs. Thereafter, antimetabolites are employed.

Testosterone propionate, a male sex hormone. is useful in treating premenopausal women with metastatic cancer of the breast.

Diethylstilbestrol, a female sex hormone, is effective against cancer of the prostate gland and against breast cancer in postmenopausal women.

MISCELLANEOUS

Actinomycin D, an antibiotic, is effective against two types of childhood cancer. Wilms' tumor and embryonal rhabdomyosarcoma, and against Hodgkin's disease.

Urethane has some effect on chronic myelocytic leukemia and multiple myeloma.

Demecolcin is useful in chronic myelocytic leukemia.

Ortho, para prime-DDD is useful against cancer of the adrenal cortex.

REORGANIZATION AND NEW PERSONNEL

The entire area of the program which had formerly been managed by a branch which we called the Field Investigation and Demonstration Branch required an entire new look because of the progressive transfer of the demonstration and control aspects of the Cancer Institute program to the Bureau of State Services under the direction of Dr. Louis Robbins.

During the fall we abolished the Field Investigation and Demonstration Branch, have been in the process of reprograming a substantial amount of its funds, and are organized now in that area for a research program pure and simple. All of the grant management functions have been consolidated under a single Associate Director, Dr. Meader, and this process of organization——

Mr. Fogarty. Dr. Meader is Associate Director of the chemotherapy program?

Dr. Endicott. He is Associate Director for Grants and Training. Dr. Sessoms is Associate Director for Chemotherapy. Dr. Shimkin is Associate Director for Field Studies, and is responsible for the research component which was formerly in the Field Investigation and Demonstration Branch. We have just announced the appointment of Dr. Zubrod as Director of the intramural research program. And these comprise the four new program Directors, all new except Dr. Sessoms.

We have also just announced a new appointment—and I think this will be very important and will help me be better prepared in the future than I am today—to the post of Associate Director for Analysis and Planning, to which we are appointing Dr. Carl Baker. And, finally, Dr. Margaret Sloan, who was the Staff Director of the study we have referred to as the Boisfeuillet Jones report, has joined my staff as special assistant for international programs.

In looking at the problems for the future in the cancer field, I would like to make a comment or two——

Mr. Fogarty. You take all the time you want to. We are not going to rush you.

PROBLEMS OF PERSONNEL AND SPACE

Dr. Endicott. Referring back to the comments of Dr. Shannon and others with regard to the problems, particularly, of personnel and of space, the Cancer Institute is really pioneering from a management standpoint in research through programs like the chemotherapy program. These have a much more positive programing implication than the normal review and approval of research grants, since in the chemotherapy program we must provide day-to-day management of a large complex interrelated applied research program. And this requires very great administrative and scientific talent.

Now I have been very depressed this year over the speed at which we are able to recruit competent people. If I have reservations as to how rapidly we can move in the future, and I do have, these reservations relate especially to our ability to recruit and keep the talents that we need to manage such programs, and to find appropriate space and facilities in which they can work.

The chemotherapy program, I think, is a good example here. We have now, I think, gotten most of our communications problems and management problems pretty well licked. The program probably can be stepped up, particularly in certain areas, and we have asked in the budget for increases for the chemotherapy program. But the worst limiting factor is not that of finding investigators to collaborate with us, but rather that of finding staff for the Cancer Chemotherapy National Service Center who can do the necessary central staff work to make this research productive in relationship to other parts of the program. This is a very serious problem for us.

Mr. Fogarty. Do they have to be M.D.'s?

Dr. Endicott. No, sir; and most of our staff are not. But in the area of therapeutic trials it is pretty difficult if they are not.

Mr. Fogarty. Well, if you have reservations about advancing very fast in this field in the next year because of personnel and space shortages, you better tell us just what you need in the way of funds for personnel and space to carry on a more effective program than this budget allows, and what will be the consequences if we do not take care of these deficiencies.

Dr. Endicott. Yes, sir.

Well, sir, the limiting factor here is not so much the money that is available to the Cancer Institute in the appropriation as it is our ability to get the staff to utilize it effectively. And this relates to other earlier testimony about personnel legislation and so forth.

Mr. Fogarty. You may supply for the record any additional information that bears on this problem.

(The following was subsequently submitted for the record:)

PERSONNEL

NIH witnesses, and particularly Dr. Shannon, have already discussed the problems related to recruiting and retaining topflight clinical and laboratory scientists at the NIH under current salary limitations. The NCI is not excepted from these problems. Although many of the NCI senior scientists are a valued heritage from the decade of the 1930's and fortunately have stayed with us, recruitment of new radiologists, endocrinologists, and other scientists has been less than fully successful, for few can afford the financial sacrifice under current salary conditions.

We would like to stress, particularly, the problem of recruiting men with scientific training and experience who have the organizational and the managerial ability to mount new activities such as the chemotherapy, virus diagnostic, and centers' programs. Some of these scientists must not only have the abilities mentioned above but bring with them a working knowledge of industrial practices. Operating a successful program has its own rewards. However, in recruiting scientists for these positions we can offer them neither the salaries comparable to those available in industry and private practice nor those satisfactions which make direct research involvement so attractive, for they must devote their time to management. We continue to experience difficulty in filling vacancies. Because of this we recommend, with the greatest of caution, the starting of new programs needing such personnel.

As indicated by Dr. Shannon, NIH has recently completed a study of its personnel problems and needs for improved conditions to recruit and retain scientific personnel. As a result of this study, proposals have been made to the Surgeon General and the Secretary and we hope to have strong support from both.

SPACE

NCI personnel are located in 10 buildings at the NIH reservation and in rented space in Bethesda and Silver Spring. Space for scientific management of new and existing programs is completely inadequate and practically none is available to provide essential laboratory backup for such programs as those in diagnosis, viruses, and carcinogenesis. Our needs will be taken care of, however, by the erection of the new cancer research building. Planning money for this building, in the amount of $700,000, was provided in the 1961 appropriation. Program planning related to this building was completed in November 1960. We are keenly aware of the urgency of starting and completing the architectural planning so that this building may be erected as soon as possible after construction money is made available.

CHORIOCARCINOMA RESEARCH

Now, in the chemotherapy area I think this year we have two very important advances. The first one has already been referred to by Dr. Shannon. This is clearly a milestone that relates to the choriocarcinoma research by Dr. Roy Hertz at the Clinical Center in the Cancer Institute. We have now gone beyond the 5-year point with a few patients without recurrence of disease. We have an overall experience of about 50 percent response to therapy with disappearance of all signs and symptoms of disease. It is prudent to be very cautious about referring to cures in cancer because they sometimes recur after long intervals. In cancer of the breast, sometimes 20 years after original surgery, metastatic disease will show up in distant parts of the skeleton and distant organs. But with this reservation I think we probably here are seeing for the first time a cure of metastatic cancer on a fairly regular basis with drugs.

Now, this is an unusual tumor. It is not really a tumor of the patient, it is a tumor of the patient's child. The choriocarcinoma that we are talking about here arises as a result of pregnancy, and the cells which make up the cancer are a part of the product of conception and are not really derived from the cells of the mother. So that this, in a sense, is a transplanted tumor in man.

Now we can cure transplanted tumors in animals——

Mr. DENTON. Where does this cancer come, in the womb?

Dr. ENDICOTT. It comes in the womb following pregnancy, sir.

But even so it is a great triumph for chemotherapy when the tumor is widespread and metastatic to be able to restore to good health a patient who would otherwise have died in a few months and to have this patient apparently cured for as long as 5 years.

CANCER OF THE BREAST

Now, there is another area which is perhaps of greater importance because it is in a common form of cancer, cancer of the breast. Choriocarcinoma is really a rare disease in the United States, but cancer of the breast is not a rare disease. About two and a half years ago, we established a study in which a drug was given at the time of surgery, when the surgeon thought he was getting a surgical cure. We randomized the cases between those who got surgery alone and those who got surgery plus a drug.

The original study included several different forms of cancer, cancer of the lung, cancer of the stomach, cancer of the large bowel and cancer of the breast.

In the first three types of cancer the drug has apparently had no effect on the recurrence rate, and there is, I think, fairly good evidence that the use of the drug at the time of surgery in the case of cancer of the lung and cancer of the stomach actually increased the mortality rate.

In cancer of the breast, however, with the first 116 patients who have now gone beyond 2 years since the time of surgery, there are some fairly decisive results emerging. I may have to come back next year and tell you not to pay any attention to it, but this year it looks very exciting to me.

The overall recurrence rate, if all the cases are lumped together, is on the order of 50 percent in those receiving surgery alone but in the group receiving surgery plus drug the recurrence rate is about 20 percent.

In young women, although the number of cases is still not large, results are even more striking. The recurrence rate in the untreated group is 54 percent, and in the treated group only 5 percent.

Now, this may be a transitory thing. Perhaps the recurrence rate will catch up with us next year, or with the next increment of 100 patients to pass through the 2-year period. But I do not really think it is going to. I think we really have something here.

The surgeons themselves are very excited about it, and perhaps too excited, to the extent that they have had serious discussions of introducing this as a standard form of therapy.

I am inclined to think perhaps it is a little early to make that decision. But at any rate, it seems quite clear that we are getting much better results with an old drug used early in the disease than we were ever able to get with that same drug used late in the disease.

The drug in question here is ThioTEPA. It has been on the record here a number of years before.

Mr. **Fogarty**. What do you mean, early in the disease?

Dr. **Endicott**. At the time of the operation.

Mr. **Fogarty**. It depends on how long before it is discovered, too; doesn't it?

Dr. **Endicott**. In part. But ordinarily the treatment that is given in cancer of the breast, as soon as it is discovered, and provided it is still localized, is an operation called a radical mastectomy, in which the breast and the lymph tissues in the armpit are dissected away. If the disease is extended well beyond the breast, then only palliative treatment is given. But for the tumors which are discovered while they are still localized, this is the treatment. This is the type of cancer I am talking about that we were treating here.

Ordinarily a patient does not receive chemotherapy for cancer of the breast until she has gone beyond the point of surgical cure, and when she has gone beyond the point where it is thought that X-ray will give her any benefit. In that situation there are no cures at all, but one gets periods of months, perhaps as much as a year of remission in which the tumor masses will shrink down, the patient will feel better and be able to get up.

Mr. **Fogarty**. What is the name of that drug again?

Dr. **Endicott**. ThioTEPA. If I might go back again to the choriocarcinoma, if drug treatment continues to work as well as it has, we believe that it won't be long before we can recommend drug treatment as preferred treatment for this disease rather than surgery.

Now it has been the practice upon making the diagnosis of choriocarcinoma if it is not thought to be spread beyond the uterus, to remove the uterus as the first treatment for choriocarcinoma. If the drug works as well in early choriocarcinoma as we think it does now, it may well be that the preferred treatment for this disease will be the drug treatment, which will be very important to young women in the child-bearing age who want to continue to have a family.

Mr. **Fogarty**. Does this have anything to do with the cytology examinations?

Dr. **Endicott**. No, sir. The cytology examination is for detection of cancer of the cervix, which is the mouth, the opening of the uterus. This disease occurs well up inside the uterus.

THE RADIOLOGY PROGRAM

Now in the area of radiation there are some fragmentary results with several different reports that suggest it may be possible to enhance therapeutic effectiveness of radiation by the use of combined radiation with drugs. The evidence is fragmentary but it is good enough, I believe, to justify rather intensive efforts in this direction.

Now here we are up against severe limitation. The limitation is in manpower and facilities. We have carried out a special study in the field of therapy radiology this year, and I am almost ashamed to report that there are only 18 residents in the United States studying therapeutic radiology today It is a 3-year course, and this means that there are six coming out in the entire United States.

Mr. **Fogarty**. Where are they?

TRAINING

Dr. Endicott. There are, I think, perhaps half a dozen places training in therapeutic radiology. The number of experienced and well-equipped investigative radiotherapists in this country is so small that it is difficult to establish a cooperative study. The equipment which is available to them varies a great deal, so it is almost impossible to set up a therapeutic protocol in which patients in one hospital can get the same kind of treatment as patients in another hospital. They do not have comparable equipment.

The National Advisory Cancer Council has recommended that we make an intensive effort in the coming year to step up training in the radiotherapy area and to develop a few—and it can only be a few at this time because of the limited number of trained people—a few additional centers for research and training in the field of therapeutic radiology. We have already made a start on this during the current year, and our plans and budget for next year provide for some increase.

Mr. Fogarty. What does a therapeutic radiologist do?

Dr. Endicott. They are specialists who treat cancer with various forms of radiant energy.

I wonder if I might go off the record?

Mr. Fogarty. You do not mean they operate a cobalt machine or something like that?

Dr. Endicott. No, sir. I mean the one who directs the operator of the cobalt machine.

Mr. Denton. I beg your pardon?

Dr. Endicott. The man who designs the treatment that is to be given by the cobalt machine.

VIRAL ETIOLOGY

Dr. Endicott. The other area I would like to mention in this brief summary is the area of viral etiology of cancer. Dr. Heller 3 or 4 years ago brought this up to the committee and pointed out that he felt there was an opportunity for an expanded program in the Cancer Institute. The committee provided additional support and at the present time the Cancer Institute is supporting virus research at the level of approximately $6 million in project grants. There have been a number of very distinguished advisers helping the Cancer Institute develop these programs. And in passing I must say that we suffered a severe loss a few weeks ago in the death of Dr. Jerome Syverton, of Minnesota, who was the chairman of one of our principal advisory committees and a leader of some of the most important research.

At any rate, it has become quite clear if we are to make much progress in the study of viral etiology of cancer, the Cancer Institute is going to have to do in this field some of the same things that it has done in the chemotherapy field. The relationship between virus and cancer is not the sort of relationship you think about in an infectious disease to which you are exposed and a few days later you come down with an acute illness of some sort, and then you are either dead or you are over it, and that is the end of it.

The viruses which we know cause cancer may be present in the animal for a very long time before a tumor appears, and when the tumor appears the virus may be gone. This we know in the animal tumors that have been established as being of viral origin. One can only suppose what may be true in man because we never have established the cause and effect relationship.

Mr. DENTON. What do you mean? I do not get that, that the virus may be gone when the tumor appears.

Dr. ENDICOTT. Well this happens in some of the experimental animal tumors.

Mr. DENTON. It would not be malignant if it was not cancer, would it?

Dr. ENDICOTT. Oh, it is a cancer, but the virus is not there. The cancer was, we know, caused by the virus, but by the time the cancer gets growing the virus is gone.

Mr. DENTON. I thought cancer was where your cells just ran amuck, they just kept multiplying.

Dr. ENDICOTT. They do.

Mr. DENTON. Then what causes the others to split that way?

Dr. ENDICOTT. The virus apparently causes a change in the cell, which alters the cell and makes it into a cancer cell which then goes on multiplying and forms a cancer. And the virus dies out.

Now this is a peculiar enough situation from a biological standpoint, but from a research standpoint it is a real mess because if you are studying cancer, you cannot be at all sure that the virus, if there is a virus that caused it, is in the tumor, or that that is the place to look.

In fact, you may have to look for the virus before the patient ever gets the cancer. Now this presents a real problem.

Another major difficulty here is that there are an awful lot of different kinds of virus. Perhaps 150 have been described up to now, and I do not know how many they turn out a week, but they are coming out. Perhaps 50 in the last 2 years have been identified, 50 new viruses. They cannot be identified by their appearance under the microscope. They often cannot be identified from the standpoint of a disease they cause because we have many so-called orphan viruses looking for a disease.

About the only way they can be identified is by the reaction between the virus and an antibody to it produced by injecting virus into an animal, and then collecting the blood serum from that animal. And as Dr. Mider mentioned yesterday, some of the cancer viruses are so weakly antigenic that they do not produce any antibody.

Now in order to avoid an enormous reduplication of effort, it is absolutely essential, we believe, to make diagnostic reagents available to researchers around the country and around the world.

We have made the first step in this direction this year. We were very fortunate to be able to continue a program initiated by the National Foundation for Infantile Paralysis. This group supported the production of diagnostic viral reagents in the class of viruses known as enteric viruses which include those viruses which produce poliomyelitis and other viruses that inhabit the intestinal tract.

We were able to pick up this program and expand it. We are arranging to acquire all of the reagents that are in the stockpile of the national foundation which is getting out of this business. And we have made preliminary arrangements to have several other types of viral diagnostic reagents produced at least in small quantity.

Now it is our plan to make these freely available to competent investigators in order to eliminate duplication of study and to accelerate the identification of new viruses and their possible relationship to cancer.

There are some other needs that are peculiar to virology. These organisms will only grow in living cells, so that they will reproduce only in tissue culture or in the intact animal. The intact animal is a very difficult thing in which to study viruses of low virulence because the animal usually has a whole flock of viruses in it already, and the relationship of the one you are studying to the viruses that are there already becomes very unclear indeed.

DEVELOPMENT OF VIRUS-FREE ANIMALS

Mr. Fogarty. What about the germ-free animal?

Dr. Endicott. The germ-free animal has been developed as one that is free of bacteria. We think, although we cannot be at all sure, that they may be relatively free of virus as well. But, as I say, the germ-free animal is free of bacteria, and not necessarily free of virus.

We have completed negotiations on a contract to attempt to develop a germ-free animal hopefully as a virus-free animal for this type of research and, if so, to design facilities, equipment, methods which will make this tool workable in the average virus lab.

Mr. Fogarty. Where would that contract be given?

Dr. Endicott. This preliminary contract will be with Microbiological Associates in Bethesda, and they would work very closely with some of the experts at the National Institutes of Health.

Mr. Fogarty. You mean there is a company in Bethesda raising germ-free animals?

Dr. Endicott. They are not now raising germ-free animals.

Mr. Fogarty. I thought there were only a very few places in the world, you and Notre Dame and——

Dr. Endicott. I think I would have to pass to someone else as to just how many there are now. That was certainly true 2 or 3 years ago.

At any rate, the problem here is not so much the raising of the germ-free animals; we can do that at the NIH; the problem is exploring its degree of virus infection, and then to develop the special techniques that might be required to maintain it in a virus-free state.

Then, finally, the tissue culture cell is the other important tool for the virologist. And here again, the more we study, the worse the picture looks. The tissue culture cell lines that we have been working with in the laboratory, many of them obviously contain, not one, but several virus contaminations that have been picked up somewhere along the line.

And here again you cannot be sure what your virus is doing if the tissue culture cell line has an unknown number of other viruses. So we have the same problem of attempting to develop cell lines, hopefully, with no virus in them. But at least, if we cannot accomplish that, to develop cell lines that have a limited population of viruses and know what the population is and what it does.

Now, obviously, we are thinking in terms of developing methodology, tools, equipment, and making them available to the investigators around the country. We hope as rapidly as possible to move this in the direction of a commercial enterprise, but at the moment there is no industry which can provide this kind of material and this kind of service. I now think we will have to subsidize and take a leading role in the early stages of the evolution of something that will some day probably be an industry.

Now this summary has been perhaps overlong in view of the hour. I have touched on a few of our problems, some accomplishments, and plans for the future. I think perhaps I should stop at this point and say that I would be very glad to try to answer any questions you have.

Mr. Fogarty. You do not have to stop. If you have anything else to say, you can say it because I think this is too important an issue to cut short.

But first I want to say, Dr. Endicott, that as head of the National Cancer Institute, even though you have only been there 8 months, I think you have done a very good job. You have given some hope, I think, to those people who have cancer.

1962 BUDGET

Now your adjusted appropriation for 1961 is $110,780,000, and the Eisenhower budget is $109,292,000, or a reduction of $1,488,000. The budget amendment increases the request to $117,167,000 or an increase of $6,387,000 over the 1961 level.

What is this "Reserve for contingencies—$1,196,800" shown in the 1961 column of the justifications?

Dr. Endicott. This is a reserve in the Bureau of the Budget of which we have already requested the release.

HISTORY OF REQUEST

Mr. Fogarty. Will you provide at this point the history of your 1962 regular request and then the history of the budget amendment, Doctor?

Dr. Endicott. Yes, sir.

(The information requested follows:)

Development of 1962 budget estimates for National Cancer Institute

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$74,181	−$8,015	$66,166	−$12,247	$53,919	−$3,508	$50,411	$62,562	$7,357	$55,205
Fellowships	2,800	−100	2,700	0	2,700	−300	2,400	2,700	300	2,400
Training	8,230	−1,175	7,055	0	7,055	0	7,055	7,055	0	7,055
State control programs	3,500	0	3,500	0	3,500	0	3,500	3,500	0	3,500
Community demonstration projects	3,000	0	3,000	−1,000	2,000	0	2,000	2,000	0	2,000
Total grants	91,711	−9,290	82,421	−13,247	69,174	−3,808	65,366	77,817	7,657	70,160
Direct operations:										
Research	14,875	−3	14,872	−225	14,647	−300	14,347	14,777	0	14,777
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	1,419	−168	1,251	+5	1,256	−9	1,247	1,560	160	1,400
Training activities	0	0	0	0	0	0	0	0	0	0
Professional and technical assistance	6,765	−446	6,319	0	6,319	−145	6,174	8,019	388	7,631
Chemotherapy contracts	21,536	+2	21,538	0	21,538	0	21,538	22,838	300	22,538
Administration	729	−98	631	0	631	−11	620	661	0	661
Total direct operations	45,324	−713	44,611	−220	44,391	−465	43,926	47,855	848	47,007
Total obligations	137,035	−10,003	127,032	−13,467	113,565	−4,273	109,292	125,672	8,505	117,167

Mr. Fogarty. What did you originally ask for?

Dr. Endicott. Well this, sir, is perhaps as confused a situation as you can find.

Mr. Seggel. $137,035,000.

Mr. Fogarty. $137 million. That is $20 million more than is in the budget.

EFFECT OF LATEST CHANGES IN BUDGET

Tell us how the reduction of $1,488,000 in the Eisenhower budget would have affected your programs and then tell us how the budget amendment of $7,875,000 will be used. That might be outdated by the time we get finished with this bill, but you can supply that for the record.

Mr. Seggel. All right, sir.

(The information requested follows:)

Effects of changes in original and revised estimates

Program activity	Net change original estimate	Increases revised estimate
Grants:		
Research	−$1,111,000	+$4,794,000
Fellowships	0	0
Training	0	0
State control programs	0	0
Community demonstration projects	+500,000	0
Direct operations:		
Research	+96,000	+430,000
Review and approval of grants	+10,800	+153,000
Professional and technical assistance	+150,000	+1,457,000
Chemotherapy contracts	0	+1,000,000
Administration	+63,000	+41,000
Reserve for contingencies	−1,196,800	0
Total	−1,488,000	+7,875,000

BACKLOG OF RESEARCH APPLICATIONS

Mr. Fogarty. What will be the total of approved but unfunded research applications at the end of 1961?

Mr. Seggel. The deficit would be, if there were no release of unprogramed funds $2,272,000 in 1961. And if we get the release which we anticipate it will be $1,775,000.

Mr. Fogarty. So if you do get the release you will still have a backlog of almost $2 million?

Mr. Seggel. This I should explain, Mr. Fogarty, reflects starting the institutional grants programs in 1961.

Mr. Fogarty. Well let's figure the backlog without that.

Mr. Seggel. According to our estimate there would be a surplus of approximately $900,000.

Mr. Fogarty. $900,000. All right.

Do you think you will have any backlog at the end of 1962 if your budget is approved?

Dr. Endicott. Yes, sir.

Mr. Fogarty. Well how many and about how much in dollars does it amount to?

Mr. Seggel. Assuming the institutional grants program does not start in 1961, but starts in 1962, there would still be a deficit of $1,830,000.

Mr. FOGARTY. Well let's assume that the institutional grant program is not started in 1962, then what?

Mr. SEGGEL. If it does not start in 1962?

Mr. FOGARTY. Yes.

Mr. SEGGEL. There would be no backlog.

CATEGORICAL CLINICAL RESEARCH CENTERS

Mr. FOGARTY. Are you familiar with the categorical clinical research centers, Dr. Endicott?

Dr. ENDICOTT. Yes, sir.

Mr. FOGARTY. Do you think they are a good thing?

Dr. ENDICOTT. Indeed I do, sir. And the multicategorical, as well.

During the late fall a number of us visited a series of institutions that had already established the multicategorical centers and had approached us as to the possibility of categorical cancer research centers as well. I had the opportunity to see some of these programs in action, or just getting ready to go into action, and to see what this meant in terms of cancer research plans in those institutions.

I think it is fair to say that most institutions actually anticipate doing some cancer research on the categorical or multicategorical centers.

Mr. FOGARTY. We used Johns Hopkins as an example the other day. Do you think they will be doing research in cancer?

Dr. ENDICOTT. To some extent, yes, sir. But their cancer research program is quite extensive and could not be accommodated in the relatively small facility which is the multicategorical center. This is what has happened elsewhere.

Now there were many limiting factors, obviously, not the least of which is the availability of space in a teaching hospital which is already overcrowded. They simply are not able, even if we had been able to provide the money, to dedicate that much of a teaching hospital to a special research facility.

But at Johns Hopkins, under ordinary circumstances, there are more inpatients being studied in our cancer chemotherapy program than 20, so that they could easily fill all 20 of the beds in that facility. The same situation will certainly occur at Duke, at North Carolina, at Alabama. These are some of the institutions we visited that have multicategorical centers, and also active programs at the clinical level.

So I think they will be most useful in the cancer field for the chemical metabolic studies which other witnesses have referred to, and especially of interest to us for intensive study of the intermediary metabolism of the drugs that we are using on an experimental basis; the absorption, distribution, excretion, and metabolism of new drugs that we have under study.

This can be carried out in an intensive fashion on a few patients in the multicategorical center permitting you to make a much more intelligent experiment on a larger scale in somewhat less elaborate facilities.

VIRUS RESEARCH

Mr. Fogarty. If you have not covered all the details in connection with virus research, will you provide it in a statement for the record?

Dr. Endicott. Yes, sir.

(The information requested follows:)

Viruses and cancer

RESEARCH DEVELOPMENTS

Major advances in research are carefully built structures of facts, painstakingly fashioned by man-years of hopes and desperation, held together by the architecture of working hypotheses. Such advances as achieve popular recognition may unfortunately be called breakthroughs, and be labeled as single-handed contributions, uncommon luck, or some happy coincidence of man and ideas. Often society fails to recognize and respect the laborious structure of the total scientific effort which made the breakthrough possible.

The gathering effort now firmly engaged in viruses and cancer research has for the past year been abuilding. It has carefully assessed its position, fashioned, new tools and procedures, looked about for more, and delved deeper into the abstruse inner meaning of the virus in its relation to the living cell. Intensive studies have been conducted in model systems of virus-induced cancer in laboratory animals, and in many laboratories across the country, the search is on for viruses significantly associated with human cancer.

Through the efforts of men of many disciplines, the virologist, pathologist, cytologist, biochemist, immunologist and their diverse colleagues, the study of viruses and cancer has multiplied its problems manyfold, and areas of increasing complexity are appearing with definition of each new facet.

The study of viruses, whether or not devoted to cancer, is extremely difficult, due not only to the size of these agents, but to the general absence of first-class tools with which to study them. The virologist must work with living and hence contaminated culture systems in the form of experimental animals and tissue culture cells. He can visualize the viruses only with the electron microscope, a huge and complex instrument, unadaptable to all but the most carefully prepared material, and then dominantly with uninterpretable results. Moreover, although the bacteriologist has reliable reagents by which to identify his "bugs," the virologist must create his own reagents at great expense. Yet in spite of this, great advances will be made, because these problems will be overcome, and the tools needed will be designed and produced for the search and study of viruses in human cancer.

Few investigators really agree as to the basic identity of viruses, but all certainly agree that a virus is essentially a mechanism by which an elaborate nucleic acid structure may transfer from one living cell to another under a variety of special conditions with a variety of results, sometimes disease, sometimes not. Most investigators favor further study of "model systems" which consist of experimental animals and known tumor viruses. However, an increasing number of scientists are now engaged in the most direct attack possible, and are working with the isolation and characterization of agents recovered from human cancer tissue. Such results as have been published thus far have been seriously challenged. None of these isolations can as yet be identified or causally related, though they are of considerable interest. A great amount of further study must be done for such work to be interpretable, and means of the routine identification of visuses on a large scale are essential. Much of the difficulty stems from the absence of a virus-free test system, either in animals or in cultured cells, as well as the lack of certified reagents for identification of viruses. The presence or absence of viruses in tumors can be most misleading.

Electron microscope studies of mouse polyoma tissues have revealed several differing viral types present in association with the cancer cells. Although other conclusive studies have shown that there is only a single kind of virus involved in causing the tumor, the presence of the other forms cannot as yet be explained. Perhaps they are chance contaminants, or perhaps they prefer the tumor tissue and have some unknown association with it. In contrast, some well-studied viral tumors often lack virus in its fully formed and recognizable infective stage. Though at first not understood, many parts of this puzzling picture are now becoming clear through study of the Rous sarcoma in chickens and turkeys, and the Shope papilloma in the laboratory rabbit.

Once a virus has entered and transformed a normal cell into a tumor cell, few or no virus particles are produced. Adjacent cells in the same tissue on receiving the virus may in sharp contrast go into a state of classic infection, in which great quantities of virus are produced, with resulting death of the cell. This has been very well demonstrated in electron microscope studies of tissues in mouse polyoma and in rabbit papilloma. If the infective cycle of a virus is either not occurring at the time, is not destined to occur, or else has run its course in the tissues so long before that the virus particles have been eliminated, then all "formed" or recognizable virus is absent. In a virus tumor at such a time, the elements of the virus are present only as an integrated part of the genetic structure of the living cell and cannot be detected with the electron microscope. Even tests of such cancer cells with the very sensitive fluorescent antibody technique may be negative.

Translating such findings to the search in human cancer, one may expect to find viruses present but of no significance in such tissues, or else find no viruses in a tumor which may actually contain elements of causative virus. New techniques are needed for disclosing the presence of viruses and revealing their ability to transform normal cells into cancer cells.

When certain viruses are stripped of their outer coat of highly specific protein, they lose their fastidious requirement for only a certain host or type of host cell. Such a stripped-down virus or "naked nucleic acid," as it is called, may be rendered infective for a much broader range of test systems. Many virologists have great hopes for this technique which is now quite well developed, first in work with the tobacco mosaic virus, and more recently with the polio group of viruses.

The mouse polyoma was the first cancer virus to be investigated by this method, and important tissue culture studies have been done. The most recent success has been achieved with the Shope papilloma of rabits in in vivo or live animal experiments. The infective naked nucleic acid of this virus inoculated in the skin of a rabbit was shown to be capable of inducing tumors which were identical with those produced by whole virus. Will such a technique reveal the cancer potential of human viruses in a host other than man? Such is the speculation of research in this subject. At least more will be known of the way in which viruses act upon cells, whether to destroy them, render them cancerous, or simply change their ability to react differently from uninfected cells. Sometimes a tumor virus, mixed with a culture of living cells taken from its customary host will produce a tumor when the mixture is injected into the brain of an experimental animal, such as a mouse or rat. This has been done with rabbit papilloma virus and with the Rous sarcoma virus of chickens. Such a method may also hold promise as a test system for candidate tumor viruses. Electron microscopy of several viruses has now reached the level of rather detailed structural studies. Perhaps most impressive has been the definition of an adenovirus as a regular 20-sided polyhedron covered by 252 protein subunits in a pattern of startling regularity. Other contributions in current research cover details of development of the virus particle itself. Some of the finest work has been done with the tumor viruses, such as the mouse leukemias.

Among the newer tumor-virus "model systems" available for study is a lung cancer in the Syrian hamster, produced by the mouse polyoma virus. Further detailed studies on mouse polyoma, mouse mammary carcinoma, the Moloney mouse leukemia, the Friend mouse leukemia and the complex of avian leukoses now offer the investigator a broad range of experimental models of virus-induced cancer. For many of these extensive studies of immunology, virus development, and mode of infection are well along. Biochemical studies have in the instance of avian myeloblastosis yielded a means of quantitating the virus by a marker enzyme, which greatly facilitates studies with this agent.

The first broad ecological investigation of a mammalian cancer virus has now been reported for the mouse polyoma, for which wild house mouse populations have been studied with fascinating results, and the modes of transmission postulated. This study may well set a pattern for surveying the viral experience of the human population in connection with cancer cases.

Another study of experimental contagion of the Rous sarcoma in flocks of chickens further adds to our knowledge of cancer viruses and the way in which they spread through animal populations.

Against this background of research progress, there are several broad areas which need special emphasis and which can soon represent critical deficits in our knowledge. Most apparent of these areas are the chemotherapy of viral disease, the survey and study of human viral experience, and the mechanisms of viral immunity.

Obvious restraining factors in the current research effort are the lack of tools and materials (viral typing reagents, defined test animals and cell culture lines, and dependable systems of procuring human tissues of highest quality for research use). Finally and most prominently, trained professional and technical people are in slow supply for this new and rapidly growing research effort.

PROGRAM DEVELOPMENTS

During the past year the research grant support relevant to viruses and cancer has grown to over $5.6 million, representing 153 projects devoted either wholly or in some significant part to this area of investigation. Following advice of the viruses and cancer panel, a board of consultants serving the National Advisory Cancer Council, several steps have been taken to insure the security and promote the effectiveness of this investment through provision of research tools and services.

Among the most pressing needs of virologists are the requirements for living reagents of the highest quality for their research. Only living cells support the growth of viruses, yet lines of cultured cells certified as to their characteristics and purity are not yet available.

Supported by research grants, a cooperative program of cell culture studies is now underway to remedy this situation. One of these grants established the Cell Culture Collection Committee early in 1960. Its first goal is through the work of its member laboratories to characterize mammalian cell lines and set up certified seed stocks free of contaminating micro-organisms and viruses so that investigators in cell and virus work may have the cell line as a high grade certified reagent. Preliminary work in the laboratory on candidate cell lines has shown the feasibility of this program.

In order to safeguard seed stocks of these certified cell lines for an indefinite period of time the committee has endorsed the use of ultrarefrigeration and has stimulated the development of liquid nitrogen refrigerators for laboratory use. These operate at temperatures colder than —170° C., and are independent of electric power.

Current participants in the new cell program include the committee's administration, two research laboratories, and the American type culture collection in Washington, D.C., as a central, national repository for the certified cells. Assisted by a grant of construction funds from the health research facilities program, the American type culture collection has made plans for a new building with considerable expansion of facilities to handle the overall needs of the viruses and cancer research for such a central repository. These facilities would also provide research space for studies related to the long-term preservation of living cells, serological reagents, viruses, and other biological materials. The Cell Culture Collection Committee is actively enlisting the aid of additional investigators in this cooperative undertaking to provide certified cell lines as dependable reagents in the virologists' testing system. Functions of the committee may be supported by both research grant and contract funds.

Virologists can now isolate some viruses rather easily and rapidly in cell cultures and in test animals, but to coordinate and correlate the information attained with that already known, the viruses must be identified, either as ones previously studied or as new agents. The only method having broad utility and dependability is serologic testing, but the reagents for such tests are not certified, extremely expensive, very limited in supply, and are not commercially available. Generally speaking, each laboratory makes its own. No laboratory can contemplate identifying viruses on a routine basis without first expending a very great effort and much money in the production of typing antigens and antisera. Such reagents, produced in individual laboratories, rarely are cross-checked, except as may be done by a few other laboratories in the course of using reference quantities in their own work, or in occasional cooperative studies.

In order to remedy this most severe shortage of tools for virology, a large-scale program was started to supply certified typing reagents, first for the viruses of man, and then as soon as they can be developed, the viruses of those laboratory animals used in virological work, especially the mouse.

As of July 1, a contract for $380,000 was begun with the Kansas University Endowment Association for the production of such serologic typing reagents as are necessary to identify the enteroviruses of man. This is a group of over 60 viruses including polio. The need for consultant direction of the enterovirus program has led to the establishment of the Enterovirus Committee, which is now actively serving the National Cancer Institute, just as those scientists have served the National Foundation in years past.

The viruses and cancer program also plans to have typing reagents produced for other viruses of man. Part of this task, that of the adenoviruses, has been assumed by the National Institute of Allergy and Infectious Diseases. Other segments may be done by other agencies and by the National Cancer Institute. The expansion of the typing reagents program to make these important tools available in large quantity for the many grantees is under consideration. Even at a comparatively high level of support, such reagents would not be produced in quantities sufficient to meet the needs for viral diagnosis study by the many students of epidemiology. Although the market for these reagents is small at present, it will certainly grow in time. Meanwhile, something should certainly be done to stimulate production.

Like the cell, the virus and the viral typing reagent, the laboratory animal is a major part of the virologist's study system. At present virologists must work with animals which are already carrying many viruses, and for which tests cannot be made, yet such extraneous agents may invalidate their research. In order that studies may be done in a clean system, and thereby be valid in their conclusions, specifically "virus-defined" animals must also be made available.

To accomplish an upgrading of the laboratory animal and establish new standards for them and for the methods and facilities needed for their handling, a Committee on Laboratory Animals has been recommended by the viruses and cancer panel and by the National Advisory Cancer Council.

The viruses and cancer panel recommends that studies in primates be emphasized. The panel suggests that as candidate human tumor viruses are discovered or put under indictment, they be tested in a laboratory animal as closely related to man as possible, and for which a broad base line of viral investigation has already been established. Such research with candidate human tumor viruses is envisioned as including the inoculation of new-born primates with viruses isolated from man and with cancer tissues from both man and primate.

To the investigator trying to link viruses to cancer in man, a most important research material is human tissue. One may be logically surprised on learning that research in human cancer actually suffers from a shortage of human material. This area of research, so important to our modern society, faces grave problems in collecting and storing the human cancer tissue needed for investigation, in such a manner as to preserve virus and prevent contamination.

Under the leadership of the viruses and cancer panel, the staff and ad hoc consultants have inquired into the problem of human tissue procurement for virus-cancer research and have found that such research is being held back because these materials are not now readily available. The problems cover the selection, removal, collection, preservation, and distribution of mature and embryonic tissues, both normal and neoplastic. The virologist seeks a tissue sample consisting of living cells rapidly removed and maintained alive with whatever viruses may be in the sample originally. Such material is not now routinely secured as a part of any surgeon's or pathologist's procedure, and so requires that they be carefully informed and assisted if such a program is to be successful.

At its meeting in November 1960, the National Advisory Cancer Council reviewed the Institute's current achievements under the viruses and cancer program, and recommended a considerable expansion of it, with full appreciation of the great problems involved.

Among the newer areas which will be emphasized by the National Cancer Institute are investigation of the principles and pilot development of facilities required for isolation of experimental animals used in viral research, the training of virologists and other investigators, provision for a more rapid and more inclusive exchange of information among research people, promotion of virus-tumor research with primates, development of certain technical equipment, and encouragement of research in viral diagnostic methods.

DIAGNOSING CERVICAL CANCER

Mr. FOGARTY. Now we have been talking about trying to find new methods for diagnosis of cancer the last few years. Are we making any headway?

Dr. ENDICOTT. We have made sporadic spurts forward, but I do not think I can report anything very exciting this year. The one example that I know Dr. Heller would want me to refer to, and so I will, is the utilization of the cervical cytologic method for the detection of cervical cancer. This is a real Public Health triumph and is an example of what can be done. But I do not have anything very exciting to report to you this year.

Mr. FOGARTY. I think Dr. Heller told us last year that this is one kind of cancer that can be almost eliminated now if women will go to their doctors at least once a year for a simple examination.

Dr. ENDICOTT. It is now a problem of public health and community management really.

DEMONSTRATION PROJECTS

Mr. FOGARTY. How much money are we spending in this field on demonstration projects throughout the country?

Dr. ENDICOTT. The total amount for community demonstration projects in fiscal 1961 is $1,500,000, and, in addition, a portion of the formula grants to States provide for this type of operation as well as part of the direct operations in the Bureau of State Services.

Now all three of these together, and perhaps including other activities, add up to about $6 million. But I can provide for you for the record a detailed report on the cervical cytology program.

Mr. FOGARTY. I wish you would. It seems to work out well in Rhode Island.

(The information requested follows:)

CERVICAL CYTOLOGY PROGRAM

The cervical cytology program of the cancer control program is directed at making the soundest and widest possible use of current techniques of preventing death and disability. Current techniques could, if used to their utmost, eliminate substantially all deaths from cervical cancer. However, it is estimated that over 12,000 women died from this cause last year. Thus, although it is reported that more than 6 million women received cervical cancer examinations last year and the death rate for this disease has fallen steadily in recent years, much still remains to be done.

To achieve the potential goal, it is essential that women—particularly those most likely to get cervical cancer—be examined periodically, and that sufficient professional and technical personnel be trained to carry out well each step in this procedure.

Program efforts, therefore, are concentrated along two major approaches:

1. Preparation of additional professional and technical personnel with skills in cytodiagnosis; and
2. Support of community projects to identify better ways of conducting casefinding programs, particularly among high risk groups.

1. *Preparation of additional skilled personnel.*—The effective use of cervical cytology requires that (*a*) family physicians be knowledgeable in ways of examining women for uterine cancer, in collecting specimens for cytologic analysis, and in managing patients with abnormal findings and confirmed cervical cancer, and (*b*) that sufficient numbers of laboratory personnel be proficient in interpreting slides. These conditions must be met in a community before there can be any assurance that all the benefits of cervical cytology will be realized.

To increase the knowledge of family physicians concerning cervical cytology, the cancer control program is working with numerous medical groups. For example, the program is cooperating with the American Academy of General Practice to encourage added emphasis on cancer detection by State and local chapters of the academy. Furthermore, financial aid has been given to a number of universities and health departments to extend training courses on this subject in both urban and rural areas. State health departments have also been encouraged to utilize funds available to them for control programs along similar lines.

The lack of enough trained laboratory personnel also limits the extension of cervical cytology. The American Cancer Society estimates that in order to double the current number of women being examined (from 6 to 12 million), about 1,200 additional cytotechnologists will be needed. Similarly, more pathologists trained in cytology will be required to guide the work of these technicians and to follow up on their findings.

To aid in rectifying this situation, the cancer control program is assisting those professional and private agencies who are seeking to increase the number of skilled cytologists and certified cytotechnologists. Grants have been made to 35 schools, including stipends for more than 300 technicians. It is anticipated that, upon completion of their training, most of these students will be equipped to supervise and train other laboratory workers. Professional groups are also being assisted by grants to strengthen their recruitment efforts and to produce better teaching materials.

2. *Support of community casefinding projects.*—Since cancer requires a team approach, involving numerous medical specialties and community agencies, demonstration casefinding projects are being aided to define better ways of enlisting women and practicing physicians in these activities. These projects emphasize methods of combining the efforts of the "team"—private practitioners, hospitals, voluntary groups, and public health and welfare agencies—who are concerned with the problem of uterine cancer. At the same time, these projects provide opportunities for increasing the number of women in high-risk groups who are examined, as well as opportunities for medical residents, family physicians, and other clinical personnel to obtain actual experience in these procedures.

To date, grants have been awarded for 15 such demonstration projects. Public and private hospitals and professional agencies as well as health departments have been recipients of these grants, which amount to more than $800,000.

Four projects are giving major attention to identifying factors that influence women to accept or to reject cytologic examinations. As in other health programs, difficulties have been encountered in arranging the active and continued participation of many women, particularly those of low income and limited education. Because these women are at special risk of this disease, the need for additional data on this issue is critical.

A major portion of the $3.5 million allocated to State health departments to assist control programs is used to aid casefinding and clinical services. More than three-fourths of the States report that these programs include examinations for cervical cancer. Increased appropriations for this purpose last year made it possible for many State and local health departments to expand these services.

The cancer control program is also concerned with extending cervical cancer casefinding efforts among persons receiving medical care at Public Health Service installations and from other public agencies. For, preventive services, such as examinations and treatment for cervical cancer, are generally recognized to be an integral part of optimum medical care. The cancer control program is therefore aiding the extension of such programs among Indian women, military dependents, and patients seen at venereal disease and other clinics. Not only will these activities help to fulfill the legal responsibility for providing preventive and treatment services for these women, but they serve as examples and models for others interested in extending skills and services in this field.

CONTINUING OBSTACLES

Although considerable progress has been made to date in overcoming obstacles to the widespread and best use of cervical cytology, there are still many communities in which needed skills and services are inadequate. Thus, to realize the full benefits of this procedure, more intensive efforts are called for to prepare personnel and to initiate programs in these areas. Only through such activities will the women and families in these isolated communities receive the advantages and protection available from this major research breakthrough in cancer control.

To spearhead a more intensive nationwide movement, an ad hoc committee on cytology has recently been organized, under the sponsorship of the American Cancer Society, to integrate the efforts of the various professional, private, and public agencies with interests in eliminating avoidable deaths from this disease. The cancer control program is participating in this work and is making its resources available to support and supplement the efforts of private and professional groups. Through the grants and consultation given to State health departments and other community agencies, similar cooperative approaches are being encouraged in localities throughout the Nation.

Through intensified efforts along these lines—to prepare needed personnel, to initiate pilot projects, and to organize comprehensive programs encompassing all interested agencies and available resources—dramatic progress can be made in overcoming remaining obstacles to the maximum use of the cervical cytology method. If these services are pushed forward steadily, the goal of preventing death and disability from cervical cancer can be achieved.

Community cancer demonstration project grants awarded specifically to further cervical cytology programs (as of Apr. 1, 1961)

State and sponsor	Subject area	Period	Amount
California:			
San Diego County, Medical Society	Cervical cancer casefinding.	July 1, 1960, to June 30, 1962.	$19,300
University of California, Berkeley	Cytodiagnostic training.	July 1, 1960, to June 30, 1962.	61,386
University of California, Los Angeles	do	July 1, 1960, to June 30, 1962.	19,346
San Diego Branch, American Cancer Society	Evaluation of public education.	Jan. 1, 1961, to June 30, 1961.	4,125
Colorado:			
Department of Health and Hospitals	Cervical cancer casefinding.	Jan. 1, 1961, to June 30, 1961.	21,890
University of Colorado School of Medicine	Cytodiagnostic training.	Jan. 1, 1961, to June 30, 1961.	9,878
District of Columbia: Department of Public Health	Cervical cancer casefinding.	Jan. 1, 1960, to June 30, 1961.	68,120
Florida:			
State Board of Health	do	Jan. 1, 1960, to June 30, 1962.	209,545
University of Florida	Cytodiagnostic training.	Jan. 1, 1961, to June 30, 1961.	24,437
Georgia:			
St. Joseph's Infirmary, Atlanta	do	July 1, 1960, to June 30, 1962.	35,130
Emory University, School of Medicine	Cervical cancer casefinding.	July 1, 1960, to June 30, 1961.	53,362
Illinois:			
East Side Health District, East St. Louis	do	Apr. 15, 1960, to June 30, 1962.	105,887
University of Chicago	Cytodiagnostic training.	July 1, 1960, to June 30, 1961.	11,370
Illinois Division, American Cancer Society	Evaluation of public education.	May 15, 1961, to Apr. 14, 1962.	8,680
Iowa: Mercy Hospital, Des Moines	Cytodiagnostic training.	July 1, 1961, to June 30, 1962.	24,127
Kansas:			
University of Kansas Medical Center	do	July 1, 1960, to June 30, 1961.	24,968
Do	Physician education.	Jan. 1, 1961, to June 30, 1961.	10,000
Kentucky:			
University of Louisville School of Medicine	Cervical cancer casefinding.	July 1, 1960. to June 30, 1962.	36,026
Do	Cytodiagnostic training.	do	18,600
Maryland:			
Johns Hopkins University School of Medicine	do	July 1, 1960, to June 30, 1961.	69,835
University of Maryland	do	July 1, 1961, to June 30, 1962.	28,623
Massachusetts: Springfield Hospital	Cervical cancer casefinding.	July 1, 1960, to June 30, 1962.	10,100
Michigan: Harper Hospital, Detroit	Cytodiagnostic training.	do	43,261
New Mexico: State department of health	Cervical cancer casefinding.	Apr. 15, 1960, to June 30, 1961.	7,000

Community cancer demonstration project grants awarded specifically to further cervical cytology programs (as of Apr. 1, 1961)—Continued

State and sponsor	Subject area	Period	Amount
New York:			
Medical & Health Research Association, New York City.	Cervical cancer casefinding.	Apr. 15, 1960, to June 30, 1961	$99,806
Memorial Hospital for Cancer and Allied Diseases, New York City.	Cytodiagnostic training.	Jan. 1, 1961, to June 30, 1961.	8,286
North Carolina:			
Bowman Gray School of Medicine	do	July 1, 1960, to June 30, 1962.	36,715
Cabarrus Memorial Hospital, Concord	do	July 1, 1961 to June 30, 1962.	15,110
Mercy Hospital, Charlotte	do	do	17,380
Presbyterian Hospital, Charlotte	do	do	20,585
State board of health	Physician education.	Apr. 1, 1961, to Mar. 31, 1962.	7,800
Ohio:			
St. Luke's Hospital, Cleveland	Cytodiagnostic training.	July 1, 1960 to, June 30, 1962.	20,010
Ohio State University Research Foundation	do	do	69,873
Youngstown Hospital Association	do	July 1, 1960, to Aug. 31, 1962.	25,500
Academy of Medicine of Toledo and Lucas County	Cervical cancer casefinding.	Jan. 1, 1961, to June 30, 1961.	1,600
Do	Cytodiagnostic training.	Do	1,950
Cancer Cytology Research Fund of Toledo	do	Dec. 15, 1960, to June 30, 1961.	11,250
Oklahoma: University of Oklahoma Medical Center	do	July 1, 1960, to June 30, 1961.	24,340
Oregon:			
University of Oregon Medical School	Cervical cancer casefinding.	Jan. 1, 1961, to June 30, 1961.	7,830
Do	Cytodiagnostic training.	do	16,700
Pennsylvania:			
Mercy-Douglass Hospital, Philadelphia	Physician education.	July 1, 1960, to June 30, 1962.	40,000
Presbyterian Hospital, Pittsburgh	Cytodiagnostic training.	July 1, 1960, to June 30, 1961.	29,300
Jefferson Medical College, Philadelphia	do	July 1, 1960, to June 30, 1962.	59,662
Hahnemann Medical College, Philadelphia	do	July 1, 1960, to June 30, 1961.	20,443
Puerto Rico: Department of Health	Cervical cancer casefinding and cytodiagnostic training.	Apr. 15, 1960, to June 30, 1962.	77,058
South Carolina: Medical College of South Carolina	Cytodiagnostic training.	July 1, 1960, to June 30, 1961.	10,690
Tennessee: University of Tennessee	do	Nov. 1, 1960, to June 30, 1962.	53,376
Texas:			
Parkland Memorial Hospital, Dallas	Cervical cancer casefinding.	July 1, 1960, to June 30, 1961.	26,392
St. Paul Hospital, Dallas	Cytodiagnostic training.	July 1, 1960, to June 30, 1962.	17,928
Hotel Dieu Hospital, El Paso	do	do	4,720
University of Texas M.D. Anderson Hospital, Houston.	do	July 1, 1960, to June 30, 1961.	39,912
Virginia:			
State Health Department	Cervical cancer casefinding.	do	57,672
Medical College of Virginia	Cytodiagnostic training.	July 1, 1960, to June 30, 1962.	19,600
West Virginia: Charleston General Hospital	do	Jan. 1, 1961, to June 30, 1961.	15,000
Wisconsin: University of Wisconsin Medical School	do	July 1, 1960, to June 30, 1961.	40,745
National agencies:			
National Committee for Careers in Medical Technology.	Cytotechnician training manual.	Jan. 1, 1960, to June 30, 1962.	20,600
Do	Cytotechnician training film.	Jan. 1, 1960, to June 30, 1961.	25,600
Board of Schools of Medical Technology	Cytodiagnostic training.	July 1, 1960, to June 30, 1961.	7,000
National Academy of Pathology	Physician education.	Jan. 1, 1961, to June 30, 1961.	9,385
Total, 59 projects			1,884,814

LOW PARTICIPATION

Mr. **Fogarty**. You say in your justification on page 79—

> The widespread application of proven techniques for the prevention of deaths from cervical cancer is being retarded by the inadequacies of current procedures as it is very difficult to enlist women to participate in case finding and follow-up activity.

Dr. **Endicott**. Yes, sir.

Mr. **Fogarty**. Why is it difficult?

Dr. **Endicott**. Well, one of the problems we have here in an action program is that we really do not know why they are not participating, and what it is that keeps women from showing up.

Mr. **Fogarty**. It might be the same reason parents won't take their children to get polio shots.

Dr. **Endicott**. That is part of it, sir.

Mr. **Fogarty**. It has to be a continual educational program.

Dr. **Endicott**. Yes, sir. And this is certainly the very heart of the cancer control program under Dr. Robbins in the Bureau of State Services.

Now we have proposed in the amended budget some increase for demonstration project direct operations. His major effort, the heart of his program, really is the cervical cytology program, the training of technicians and pathologists to do this kind of examination, demonstration projects to educate the communities, continuing efforts working with physicians as well as the public in order to hammer home the educational lesson here that, "This is how you do it."

Now I am very impressed with the effectiveness of Dr. Robbins, his program and his staff, and I think if anyone can do a job on this they will.

Mr. **Fogarty**. But no other diagnostic tools have been developed in the last year?

Dr. **Endicott**. Not of any real consequence, sir, no.

Mr. **Fogarty**. I received an invitation last evening to attend a function here for Dr. Papanicolaou. He is the man responsible for this?

Dr. **Endicott**. Yes, sir. As you know, he has received the Lasker Award, and perhaps he will achieve even greater distinction one day.

Mr. **Fogarty**. I hope so.

GEOGRAPHIC AND RACIAL DIFFERENCES IN CANCER INCIDENCE

What about the geographical and racial differences in cancer incidence? Do you know any more today than you did a year ago, or 2 years ago?

Dr. **Endicott**. Yes, sir. Evidence there is accumulating so fast it is hard to sort it out. Here are many opportunities, I am sure, for research leads if one can relate population differences and geographical differences to something significant in the environment. Our efforts have become rather extensive in this field thanks largely to the work of Dr. Shimkin, Dr. Haenszel, and Dr. Cutler.

Some years ago we established a very fruitful collaboration with the State of Connecticut, and have made intensive long-term studies of the natural history, the incidence and so on of cancer in Connecticut. Thus is a first-rate State registry of cancer. It also has first-rate vital statistics.

Some 3 or 4 years ago this was extended to other States and other hospitals around the country. About a year ago it was extended with registries in the Scandinavian countries and England. We are hopeful that we will be able to extend this to include collaboration with the Russians, the Japanese and a few other areas.

Now to be really effective from a statistical standpoint, one needs a number of basic factors. One needs to know the age distribution of the population, the birth rate, the death rate, the cause of death and so forth. There are very few countries in the world doing any kind of a job at all in these areas. So that in many of the backward countries they have no notion of the death rate, the birth rate, the cause of death, or the size of population.

It is not very meaningful, in the absence of all the other data, for one to go to a hospital and collect a few isolated statistics about cancer coming through that hospital. So that in many instances the statements which you hear, that something is very high in Abyssinia and very low in Chile, may be more of an impression than anything else.

Now as I say, we have a lot of information on relative incidence of this or that kind of cancer in one country or one area versus another country or another area. But some of it is pretty shaky. And our success in this area is going to depend a lot on what some other people do in programs like ICA, for example, in establishing adequate vital statistics programs in some of the other countries.

Mr. Fogarty. Do you think the ICA is capable of it?

Dr. Endicott. Yes, sir; and they are doing a very good job in some areas already.

Only a few of the States have a statewide cancer registry. The oldest, I think, is Connecticut. I may be wrong about this. Connecticut, Massachusetts, Texas, California—the States that we have worked with mostly. The California coverage is very partial. They are just spotted, selected areas. It is not statewide.

Many States have no statewide registry of any sort.

Mr. Fogarty. What about Rhode Island?

Dr. Endicott. I think Rhode Island does not have a statewide cancer registry.

Mr. Fogarty. Why shouldn't they have it?

Dr. Endicott. It would be quite useful.

The custom has been to develop tumor registries around a hospital, and each hospital then makes a registry of the patients that have come to that hospital and attempts to follow them up. And with the mobility of citizens of the United States this becomes a very difficult thing for a hospital to do. They lose track of their patients so easily.

INTERNATIONAL RESEARCH

Mr. Fogarty. What are you doing in the field of international research?

Dr. Endicott. The National Cancer Institute has had extensive international enterprises for a long time. There is an international organization, the International Union Against Cancer. I think it is appropriate to say this has resulted largely from the activities of Dr. Heller and his staff. We have supported a number of research projects for a good many years. As a matter of fact, the last thing I did in the Cancer Institute, before I went with Dr. Shannon's staff, was to spend a month in Japan organizing a fairly extensive collaborative program with the Japanese in the field of chemotherapy. This year we have expanded our support abroad. We have a number of applications which have been recommended and which will be paid as money becomes available, and we are developing a number of collaborative programs using the foreign currency funds. To a large extent these funds are being utilized in programs which involve the collaboration of scientists on the Cancer Institute staff with scientists in the other countries.

Dr. Sloan, who came to us a month or so ago, is searching for the right combination in which perhaps the Cancer Institute can develop a pattern somewhat like that now being developed in National Institute of Allergy and Infectious Diseases, which will be particularly suited to the Cancer Institute's problems.

Now as I mentioned before, we have interest in some of the backward countries, and there are undoubtedly research opportunities there. We have some growing programs in some of the countries which are not necessarily backward, but which have blocked currency. Unforunately, the great research strength in the cancer field is in advanced nations which do not have Public Law 480 funds. They are in countries of Western Europe, the British Isles, the English-speaking population of the world in general, and perhaps a few countries like Japan.

Mr. FOGARTY. Israel is doing——

Dr. ENDICOTT. Israel is certainly an outstanding research nation.

Now the programs and institutions that are concerned with tropical disease, infectious disease, parasitic disease, tend to be in different parts of the world than the Cancer Institute would normally deal with. So we are groping for a special pattern.

EXAMPLES OF RESEARCH ABROAD

Mr. FOGARTY. Do you have examples of any of these foreign countries that we are doing business with who are helping you out in any way?

Mr. LAIRD. That have made grants to people or institutions in the United States.

Dr. ENDICOTT. Yes, sir. As a matter of fact, there have been grants in the cancer field, and especially from England. They have old, well-developed programs and have made grants in the United States.

Mr. FOGARTY. What other contributions have they made to advance this field of research?

Dr. ENDICOTT. Well, this morning when I left the office there were two members of my staff and a man from Sweden who wanted to see me, and could not today, to talk about an interesting development in Sweden, in which the Swedes will do the clinical investigating if we can help them out with the laboratory side.

Dr. Bjorkland, from Sweden, is an immunologist of some distinction and has been doing a series of experiments using human tumor tissue, injecting it into horses and collecting serum in order to study whether he could produce any immunity agains cancer.

In the horse serum there are antibodies which react to substances in human tumors, and they react with substances in hela cells which are one of the common tissue culture cell lines used extensively in this country. It is thought that we can probably use the hela cell as the antigen to produce and to standardize antigens which would then be utilized in Sweden as a immunizing agent in carefully selected and paired populations of rather elderly patients whose cancer expectancy is high.

Mr. FOGARTY. I know you have many other examples.

Dr. ENDICOTT. Yes, indeed.

Mr. FOGARTY. Please supply a few for the record.

(The examples requested follow:)

EXAMPLES OF BENEFITS FOR CANCER RESEARCH DERIVED FROM PARTICIPATION WITH AND SUPPORT OF FOREIGN SCIENTISTS

One need only recall a few of the major developments that have been so important in improving the health and welfare of mankind to illustrate the international scope of biomedical research: Pasteur (France)—development of the germ theory and establishment of the field of immunology; Virchow (Germany)—founding of the field of pathology, thus allowing accurate diagnosis of disease; Reed (United States)—demonstration of mosquito transmission of yellow fever; Ehrlich (Germany)—founding of chemotherapy; Yamagiwa and Ichikawa (Japan)—production of experimental cancer by means of an environmental chemical; Banting and Best (Canada)—isolation of insulin and treatment of diabetes; Fleming (Great Britain)—discovery of penicillin.

Cancer research, like other areas of medical research, continually benefits from current investigations conducted by foreign scientists. Scientists in the United States gain from association with foreign scientists through: (*a*) findings and products obtained from their investigations; (*b*) exchange of information and new concepts; (*c*) knowledge gained from studies not possible in the United States; and (*d*) training received by American scientists with outstanding scientists in other countries. Often these foreign scientists are significantly assisted in making their contributions because of financial support received from National Cancer Institute grants.

To illustrate some of the benefits to cancer research and to U.S. cancer investigators, a few examples of research studies conducted in foreign countries are cited.

VIRUSES AND CANCER

One of the outstanding centers of research on viruses and cancer is the Institut de Recherches sur le Cancer, Villejuif (Seine), France, until recently under the direction of the late Prof. Charles Oberling, one of the pioneers in virus-cancer investigation. Particularly noteworthy have been the superb electron microscopy studies of tumor viruses by Bernard and Hagenau. Numerous American investigators have benefited from visits to this institute, and both of these scientists have worked in our laboratories on studies of joint interest.

One of the foremost laboratories studying the structure and synthesis of viruses and their nucleic acid and protein components is the laboratory of Schramm at the Max Planck Institute for Virus Research, Tubingen, Germany. Important collaborations with American scientists continue to further our basic knowledge of viruses.

Outstanding among those investigating the interaction of viruses and cells are Lwoff, Jacob, and Monod at the Institut Pasteur in Paris. Not only have the many superior research publications produced in this institute greatly increased our understanding of virus infection, but visiting scientist positions in the laboratories of these investigators have become eagerly sought by numerous U.S. scientists.

STUDIES ON CANCER IN POPULATIONS

Several studies are underway to obtain definitive statistical information on cancer in countries that do not have these data. In many foreign countries the incidences of cancer in the various body organs differ from those of this country, and leads as to the reasons for the differences are sought in the studies.

Clemmesen, at the Danish Cancer Registry in Copenhagen, who is one of the world's authorities on the epidemiology of cancer, is collecting statistical information on cancer in Denmark and is also making worldwide comparative studies. This Registry, like several others throughout the world, is collaborating directly with staff members of the National Cancer Institute in order that data collected in many countries are obtained in like fashion and can be directly compared. A few important studies, such as the one by Janz and Prates at the Institute of Tropical Medicine, Luanda, Angola, are in progress in Africa where cancer incidences for certain organs, e.g., liver and esophagus, are quite different from those seen in other areas. Investigations are being conducted in Germany, England, and other countries on cancer incidence among workers in certain industrial environments, including collection of data on possible harmful environmental agents.

CANCER INDUCTION

One of the key observations related to the process of induction of cancer by chemicals is the demonstration that certain chemicals not carcinogenic in themselves will increase cancer-inducing potency of carcinogenic agents. This phenomenon, called cocarcinogenesis, was pioneered by Berenblum, now at the Weizmann Institute of Science, Rehovoth, Israel, and additional work by this investigator on the mechanism of carcinogenesis is of high interest to a number of American cancer investigators. A unique study is being conducted by Horta at the Faculdade de Medicina de Lisboa, Lisbon, Portugal, of individuals who had received Thorotrast, a substance once used in X-ray diagnosis because it is opaque to X-rays but also of potential danger because it contains radioactive thorium. Mori-Chavez at San Marcos University in Lima, Peru, and formerly a visiting scientist at the National Cancer Institute is evaluating the effects of high altitude on cancerous growth in experiments conducted high in the Andes. Miyaji, also a former visiting scientist at the National Cancer Institute, now at Osaka University Medical School in Japan, is studying relationships between cirrhosis and liver cancer, utilizing unique conditions in Japan. Haddow and Bergel, at the Chester Beatty Institute in London, are contributing important research findings on carcinogenesis, and many American cancer investigators have profited from visits with these British scientists.

METABOLIC AND BIOCHEMICAL STUDIES

One of the world's outstanding endocrinologists, Houssay, Nobel Laureate at the Instituto de Biologia y Medicina Experimental in Buenos Aires, is investigating the role of endocrine glands in cancer and other diseases. On two occasions, Professor Houssay spent some time working in the laboratories at the National Institutes of Health. Caspersson, a distinguished investigator at the Karolinska Institutet in Stockholm, employs advanced optical techniques and other cytochemical methods to study protein metabolism of cancerous and other cells; numerous investigators from the United States have received valuable advanced training at this institute. Several outstanding investigators are making important contributions to understanding in basic biochemistry: Sanger in England on the detailed structure of insulin and other proteins; Lynen in Germany on metabolic pathways; Khorana in Canada on the synthesis and metabolism of compounds related to nucleic acids; Crick and Kendrew in England on theoretical models of proteins and nucleic acids; Pullman in France and Coulson in England on electronic molecular structure in relation to carcinogenesis; Katchalski in Israel on synthesis of large polymer molecules of biological interest. The laboratories of these investigators likewise provide important training for many scientists.

IMMUNOLOGY

In addition to the work of Björklund mentioned above on the immune lysis of human cancer cells, other investigations conducted overseas are of high importance. The most recent Nobel Prizes in Medicine to Medawar in England and Burnet in Australia are indicative of the importance and high interest in immunology, and transplantation immunity and acquired tolerance have special significance to such areas of cancer research as tumor transplantation; metastasis, tumor progression, and viruses. Gorer of Guy's Hospital, London, continues to make important contributions on tumor immunity, tumor progression, and on knowledge of genes involved in transplantation immunity. Zilber of the Institute of Epidemiology and Microbiology (Gamalei), Moscow, U.S.S.R., is reporting valuable research findings on tumor antigens and oncogenic viruses.

CANCER CHEMOTHERAPY

A number of chemotherapeutic agents have originated in foreign countries: (a) cyclophosphoramide (an alkylating agent currently in use for the management of reticulum cell sarcoma, lymphosarcoma, acute leukemia, and Hodgkin's disease—developed at the Asta-Werke Co. in Bielefeld, Germany, and introduced in the United States through the Mead Johnson Co.; (b) myleran (an alkylating agent useful in the treatment of chronic myeloctic leukemia)—originated at the Chester Beatty Institute in England and commercially produced by Burroughs-Wellcome Co.; sarcolysin (an alkylating agent useful in therapy of seminoma of the testis and a few other tumor types)—originally synthesized at the Institute of Experimental and Clinical Oncology, Moscow, U.S.S.R.; nitromin (an alklyating agent reported by Japanese physicians to be beneficial in several types of cancer; it is currently being evaluated in clinical trials in the United States)—originated in Japan.

Several groups in Europe are participating in the Cancer Chemotherapy National Service Center clinical trials program as part of the European Cooperative Breast Cancer Group (Belgium, France, Germany, Italy, and Switzerland). Haddow and Bergel in London, Lettre in Heidelberg, Lavie and Gitter in Rehovoth, and Yoshida in Tokyo are among foreign investigators making important research contributions to cancer chemotherapy.

Other examples could be cited. Significant cancer research potential exists in other foreign areas, such as India (epidemiology and preparation of agents for chemotherapy), Japan (studies on stomach cancer and chemical syntheses), southeast Asia (choriocarcinoma and epidemiology studies), Africa (studies on epidemiology and bladder, liver, and esophagus cancers) and South and Central America (clinical evaluation of chemotherapeutic agents).

FELLOWSHIP AND TRAINING PROGRAM

Mr. FOGARTY. There is no change in the fellowship and training budget from 1961; is there?

Dr. ENDICOTT. No, sir.

STATE CONTROL AND COMMUNITY DEMONSTRATION PROGRAMS

Mr. FOGARTY. Is there any thought of transferring the State control program and community demonstration projects to the Bureau of State Services budget?

Dr. ENDICOTT. This has been discussed, I am sure, and I do not know what the present thinking is. Perhaps Dr. Terry would be able to comment on that.

Dr. TERRY. I know of no plans to change it for the Cancer Institute.

Mr. FOGARTY. All right. Will you tell us then for the record what is currently being done under these programs, and whether you plan any significant changes for the future?

Dr. ENDICOTT. Yes, sir.

Mr. FOGARTY. You can supply that.

(The information requested follows:)

ACTIVITIES OF THE CANCER CONTROL PROGRAM

The cancer control program in the Bureau of State Services assists State and local agencies, practicing physicians, and allied workers in applying and utilizing practices which can prevent deaths and disabilities from cancer. To accomplish these objectives, the program administers two grant programs: one to aid State health department control programs and the other to assist community demonstration projects. The program also provides professional and technical assistance to help in planning, carrying out, and evaluating community programs.

The work of the cancer control program is based on the assumption that the practicing physician is the key to effective cancer control in the community. Acceptance and utilization of a scientific breakthrough comes, not through formal publications and official pronouncements, but through the growing realization of local practitioners that the new procedure constitutes good medical practice and should be available to his patients. This step is all important in the application of research gains. However, it can only be hastened by involving medical practitioners actively in the planning and conduct of operating programs at the National, State, and local levels.

Grants to State health departments for strengthening control programs are used for such services as the provision of professional and public educational programs, the support of clinics and home nursing, the maintenance of registry systems to improve patient followup and care, and program direction. In fiscal year 1961, this grant was increased for the first time in over a decade—from $2,250,000 to $3,500,000. The formula for distributing this money among the States was adjusted so that each State receives at least $25,000. This increase has been utilized by most of the States to strengthen examination and diagnostic services.

Grants for community demonstration projects were initiated in the fall of 1959 to facilitate the application of confirmed techniques in community programs. To date, about 100 grants, amounting to more than $2,300,000, have been awarded. These awards are made after review and recommendation by a committee of non-Federal medical consultants with experience in various aspects of cancer control. The approved projects have been carefully selected from approximately 200 applications. The expanding interest and participation of an increasing number of agencies in this work—hospitals, universities, professional agencies, and health departments—has been one of the most significant developments.

The majority of the community demonstration grants awarded to date have been to strengthen cervical cytology services. Fifty-five grants amounting to about $1,100,000 have been concerned specifically with increasing skills in cytodiagnosis. Nineteen grants for demonstration case finding projects, amounting to about $800,000, have been approved. Other projects are directed at the organization of programs to advance the skills of family physicians in other cancer-detection practices, the analysis of data on trends in cancer mortality and morbidity, evaluation of public educational programs, and the development of better materials on the rehabilitation of cancer patients.

The professional and technical assistance activities of the cancer control program include (1) consultative services to State and local agencies in medicine, nursing, dentistry, education, statistics, and related fields, and (2) operational studies to identify better ways of using confirmed practices under field conditions, and (3) educational programs to advance the skills of various professional and technical personnel responsible for cancer control work.

In line with the basic approach of the cancer control program, special emphasis is given to achieve the maximum involvement and participation of practicing physicians in these activities. This is essential to insure that programing is developed on a sound basis and that recommended practices are, in fact, adopted and put to routine use. One method that has been found most effective has been the sponsorship of medical discussion programs, in cooperation with the American Academy of General Practice. Cancer problems in office practice are discussed by small groups of family physicians who are responsible for coordinating family medical care and early cancer detection; medical specialists assist as needed. This affords the practitioner an opportunity to exchange views with associates and with specialists on the practical problems of applying cancer-control techniques. Tape recordings of these sessions are useful in stimulating additional discussions by other groups of physicians; thereby extending the number of practitioners involved in these programs and procedures.

The cancer control program is also giving major attention to evaluation studies to improve the operations of ongoing programs. This approach is concerned both with experiences in the community, the clinic, and the laboratory. Difficulties encountered in winning the participation of women in casefinding programs are being explored with the aid of social science research specialists. Better ways must be found to win the acceptance of women with varied educational and social backgrounds of recommended examinations and treatment. In another area, studies of better techniques of preparing and interpreting specimens in a large-scale operating laboratory are being carried out so as to improve the efficiency and accuracy of these services.

While primary attention is focused on the extension of cervical cytology activities, the cancer control program is also furthering educational programs concerning scientific findings on the relationship between smoking habits and the risk of lung cancer. These activities are in line with the policies outlined in the Surgeon General's statement on "Smoking and Lung Cancer." These programs are being extended to help professional groups bring data on this problem to the attention of their members and to high school and college students.

These approaches provide a variety of tools for meeting and overcoming obstacles to the sound and full use of findings that can reduce disability and death from cancer. As these resources are strengthened not only will they be able to make better use of current knowledge and practices but they will be prepared to handle effectively the additional prevention and control measures that are likely to emerge from the major research efforts now underway.

For example, several new opportunities for cancer control, offering promise of substantial reduction in the death rate, are nearing the stage of being "practice ready." The further demonstration of the value of mammography as a technique of identifying breast cancer through X-rays prior to biopsy may provide an effective tool in a major area of cancer disability. The wider use of proctoscopy to detect cancers of the colon-rectum needs further exploration to determine practical problems of application. Current investigations of the use of cytology in diagnosing cancers of the stomach, colon, and oral cavity may provide findings of great value for future control efforts. Similarly, continuing educational programs for family physicians will be called for as progress is achieved in the promising field of chemotherapy.

As research breakthroughs in these and other areas are confirmed, the professional and financial resources of the cancer control program will offer tested and flexible methods both of identifying practical problems in putting these practices into widespread use and of involving practicing physicians and community agencies in overcoming these obstacles. In this way, such gains can be exploited to their full human benefit with the minimum possible delay.

ALLOCATION TO VA

Mr. Fogarty. You are allocating $768,000 to the Veterans' Administration?

Dr. Endicott. Yes, sir.

Mr. Fogarty. They have a pretty big research program of their own, don't they?

Dr. Endicott. Yes, sir; they do, and a very fine one.

This is a working account which we have established to pay a part of the cost of the expense of therapeutic trials being carried out for us in the Veterans' Administration hospitals. They provide a very, very large part of our entire therapeutic trial apparatus in the chemotherapy program. This is just a very small part of the cost.

Mr. Fogarty. What do you expect to allocate to them in 1962?

Dr. Endicott. The present plan is to make the same allocation.

Mr. Fogarty. If it is that good a program, why don't you step it up some?

Dr. Endicott. Well, sir, we have been able to get them to step it up without asking for more money.

CANCER IN ANIMALS

Mr. Fogarty. We are now giving physical examinations to cows for hints on the basic nature of leukemia. This was reported at the meeting in St. Petersburg. I suppose this would be laughed at by many who are looking for something to ridicule; but I imagine it must be important or they would not be reporting on it. They say that leukemia in cattle is very closely related to the disease in man.

Dr. Endicott. Well, sir, I did not mention it in my testimony, but it is an area which I think is of great importance for future exploration, and this is the whole area in the study of cancer in the animal populations. Now this is going to become increasingly important as we come nearer and nearer to pinning down, and I am sure we will, viral etiology in the cancer field. There is little question in my mind that we will, some years hence, be talking about the same sort of thing in the cancer field that Dr. Shannon was talking about yesterday in the malaria field.

Animals have cancer, all kinds of animals have cancer, and many of them look exactly like the cancers that man has. We know very little about animal cancer except in those few animals that are domesticated, where it presents an economic problem. And this is clearly true especially with cattle. Cancer causes serious economic losses in chickens and turkeys and cows.

Mr. Fogarty. How about pigs?

Dr. Endicott. Pigs?

Mr. Fogarty. Generally if there is something that is killing pigs, the Department of Agriculture spends millions of dollars trying to find out what causes it.

Dr. Endicott. Well, pigs have a low incidence of cancer and there is something that perhaps explains this. They do not keep pigs very long. Most pigs are killed when they are fairly young. Cancer is not a particularly pressing problem amongst swine.

HEPATOMA IN TROUT

But this year we ran into an interesting new one. I thought it was probably going to make some wild headlines, but it did not. There was an outbreak of hepatoma, which is a liver cancer, in the rainbow trout of the West. This was first detected in shipments of rainbow trout moving from the hatchery in one State to public fishing ponds in another State.

The incidence was extremely high. And this started a series of studies of hatchery trout with a startling incidence of cancer of the liver in the older trout in the hatcheries. We do not know yet what causes this.

Mr. Fogarty. I thought one of your men suggested that might have been caused by a radical change in diet?

Dr. Endicott. Yes, sir. And this may well turn out to be the case. But it is far from established at this point. We have several active projects going on this. But it is an excellent example, I think, of what I am talking about. This has reached epidemic proportions in one species of food animal. In some hatchery populations as many as 60 to 80 percent of all of the trout have cancer of the liver.

POSSIBLE ROLE OF NUTRITION

Mr. Fogarty. What about nutrition? Does any kind of diet cause any kind of cancer?

Dr. Endicott. Well, sir, there is unmistakable evidence that you can produce certain forms of cancer by the injection of certain kinds of chemicals. Whether it is nutrition in the ordinary sense, that is, eating a little too much imported cheese or something of that sort, that is more of a moot question. There is fair evidence that certain nutritional deficiencies will produce cancer, particularly cancer of the liver if there is deficiency of essential amino acids of the B vitamin group. This is coming to be a very uncommon nutritional deficiency in the United States so it is probably of not much importance to us.

KREBIOZEN

Mr. Fogarty. Before we finish this appropriation, we want you to bring us up to date on krebiozen. Because we are running a little late we will ask that you put a statement in the record.

(Information on krebiozen was furnished as follows:)

Clinical Evaluation of Krebiozen

For the past 2½ years the National Cancer Institute has been activately engaged in discussions and correspondence with Dr. Andrew C. Ivy and Dr. Stevan Durovic concerning the possibility of arranging for clinical evaluation of krebiozen as a treatment for cancer. These exchanges were started in 1958 by Dr. John R. Heller, and have been continued since the present Director of the Institute assumed office last July.

The committee is probably aware that the main topic of these discussions has been the procedure under which clinical evaluation might be undertaken or sponsored by the National Cancer Institute. Last October conferences were held with Drs. Ivy and Durovic and agreement reached upon the first step to be taken toward organizing clinical trials. It was agreed that all of the available pertinent data obtained by individual physicians who have used krebiozen for research purposes should be summarized in a usable form for those who would be responsible for designing and conducting further studies involving human patients. This procedure could lead to clinical trials which would produce definitive results.

At the October conference Dr. Ivy indicated that he would undertake thus to summarize the data. He could not set himself a precise deadline for the completion of this task, because it is understandably a large one. Krebiozen has been made available to doctors for research purposes for about 10 years, and their data are voluminous. The information has not yet been received, but Dr. Ivy has given assurance that he hopes to complete his task before long.

The discussions with Drs. Ivy and Durovic were entered into to bring this matter toward a definite conclusion. As soon as the summary which Dr. Ivy is preparing is received, the National Cancer Institute will be able to take the next step, which will be to determine what these data offer to those who would undertake to design and conduct the studies constituting the final phase of the procedure.

METHOTREXATE

Mr. Fogarty. I have a couple newspaper clippings here. This says, "New Drug Fights Cancer in Kenya—U.S. and British Physicians To Further the Use of Methotrexate in Africa." The work will be financed by the African Research Foundation and the Sloan-Kettering Institute of New York.

Dr. Endicott. We are not financing it; but this is a study of a response to one of the older drugs, methotrexate. That is the same drug Dr. Hertz used to treat choriocarcinoma.

Mr. Fogarty. Made at Lederle?

Dr. Endicott. Yes, sir. I believe most of the work has been done by Dr. Sullivan from New York City, who has been out to Kenya and has had some very good therapeutic results in cancer of the throat which occurs almost in epidemic proportions in children there in the colored population.

Mr. Fogarty. I think it is a 2-year study according to this report.

POSSIBILITY OF AN ANTICANCER VACCINE

Dr. Heller was quoted in Oklahoma in December as saying:

> Vaccines have already proved up to 95 percent effective in preventing some animal cancers. And it is possible that vaccination will be the answer to cancer in humans.

Dr. ENDICOTT. I think he is probably talking about the Friend virus which was isolated by Dr. Charlotte Friend at the Sloan-Kettering Institute. It causes leukemia——

Mr. FOGARTY. This is just——

Dr. ENDICOTT. That is a speculation.

LEUKEMIA

Mr. FOGARTY. Have you made any headway in leukemia? They have been able to keep these children alive longer than they were 7 or 8 years ago, haven't they, because of the use of these new drugs?

Dr. ENDICOTT. Oh, yes.

Mr. FOGARTY. Many are living 2 or 3 years instead of 6 weeks?

Dr. ENDICOTT. It keeps inching up and inching up as you get a larger and larger battery of chemicals that you can try after the old ones fail.

Mr. FOGARTY. That is what Dr. Farber has been doing in Boston for some years now.

Dr. ENDICOTT. Yes, sir. They have had several new ones coming along in the last several years that are active in acute leukemia, and it is too early to tell what their impact will be on the overall survival rate. But I am reasonably confident it will be the same story, that a couple of years hence we will say the application of these new drugs has lifted it a few more months. But there is no startling breakthrough.

CONTACT WITH RUSSIAN SCIENTISTS

Mr. FOGARTY. Now here is another newspaper story:

> Russians report new cancer clue—antigen is believed isolated from tumor in stomach, scientists say here—five specialists on visit—exchange group is guest of memorial center—trip to National Institute set.

This was in September last year.

Dr. ENDICOTT. Yes, sir. We had a visit——

Mr. FOGARTY. "Tests on human stomach cancer subjects in the Soviet Union have established that a specific tumor antigen is present, it was reported here yesterday."

It was reported by our people and not by them.

Dr. ENDICOTT. Yes. The Russian group, and I think there were five of them, visited New York at the Sloan-Kettering Institute and the Cancer Institute in September. These were a series of very distinguished scientists. We had known several of them for a good many years through contacts with international meetings. They stayed several days in each place, saw some of the work we were doing, and most of them made some presentation of their own work and progress.

We have arranged for seven of us to visit in Moscow beginning around the 27th of May of this year, and visit some of their leading centers. There is another group of Russian cancer scientists scheduled to arrive here next week to visit at the Cancer Institute and other institutions in the country. And we have now just about completed arrangements to send one of our younger scientists to spend 6 months to a year in Russia doing some research with some of the Russian investigators.

The pace of exchange of information of people is accelerating.

Mr. Fogarty. Is that good?

Dr. Endicott. I think it is, sir. I have not been to Russia yet—I am going in May—but it is my distinct impression that in the broad field of cancer the United States is far in the lead, and that our lead is not even threatened. But there are a few areas in which they are doing a first-rate research that we ought to know about. We ought to know about it sooner, and we ought to know more about it.

And one of these areas is chemotherapy. They are synthesizing and developing good drugs over there. They are doing it simultaneously with us and with the British in some instances. And I would not for a minute underestimate their ability to step this up in the future. They have first-rate chemists there.

Mr. Fogarty. Mr. Laird.

DURATION OF GRANTS TO FOREIGN GRANTEES

Mr. Laird. Dr. Endicott, I note that one of your 10 largest grants was to the Royal Cancer Hospital in London, England. This grant was approved to run through December of 1962. Are these foreign grants made on a yearly basis? That is, they understand these are on a yearly basis, do they?

Dr. Endicott. Oh, yes.

Mr. Laird. This is not true with some of your grants that are in your international research program under Public Law 480? Some of those grants are made for more than 1 year, isn't that correct?

Dr. Endicott. Well, our grants are all made for 1 year——

I am sorry, I misunderstood your question. The Public Law 480 funds are quite different. I did not understand them myself. I am sure Mr. Kelly could help you.

Mr. Laird. I understand them. But I want to find out if this one is handled in the same way as the grants are to investigators in the United States.

Dr. Endicott. That is right.

Mr. Laird. On a yearly basis. And it takes action by the Congress as far as appropriations are concerned to assure that they will be continued?

Dr. Endicott. Yes, sir.

Now there is one slight difference that I might mention here. It would not apply to this one, but it would apply, let's say, to a grant made in Palestine. We attempt to find, before we award one of these grants, where there are foreign currencies available to determine whether part or all of the grant may not be made in the foreign currency. And this grant procedure has just been set up, I think, and is just beginning to work.

Now I could not answer, and I would have to turn to Dr. Price or Mr. Kelly as to what this would mean in terms of the fiscal years and so on. That might make some change. But if the grant is in dollars, it is made on exactly the same basis it is to domestic grantees.

POSSIBLE USE OF FOREIGN CURRENCIES IN LIEU OF DOLLARS

Mr. LAIRD. I notice in your justifications for the Public Law 480 program, on page 199, that a statement is made, and I quote:

> Likewise these funds will not be used to support projects which would normally be eligible for support from dollar appropriations.

Now last year during the hearings I conducted a little questioning on the advisability of your investigating rather closely to see if counterpart funds could not be used in these cases. I want to know what progress you have made since my questioning of Dr. Heller last year?

Dr. ENDICOTT. I will have to ask the question of Dr. Price. These negotiations have been handled at his level. I think they are coming along very well, as a matter of fact.

Dr. PRICE. Well, the citation which you have just read from the justification refers to the particular program authorized under Public Law 480.

Mr. LAIRD. I should think that sentence would read just the other way around. If you were actually going to use the counterpart——

Dr. PRICE. What we are attempting to do in the case of other parts of our program—let me say it this way: Before we ever had this kind of a Public Law 480 program set up, we were making grants under the cancer program, the heart program, and others to investigators in foreign countries. The newly authorized activity which we propose to handle, as the justification points out, and as you will hear later when this particular program is discussed with the committee, is an extension of our intramural research activities at Bethesda. But we have been making grants to support investigators abroad under our regular programs and using our hard currency programs——

Mr. LAIRD. My questions last year were directed to why we did not start substituting soft currency for dollars.

Dr. PRICE. We have now taken the steps to do this wherever those currencies are available to our Government.

And now we have established a procedure so that wherever we have a grant approved, or payment in a foreign currency, we check to see whether or not local currencies are available to our Government and use those to pay the grant wherever this is feasible.

Mr. LAIRD. Your explanation is just the opposite from the statement I read from your justifications.

Mr. KELLY. Not quite, Mr. Laird. We are drawing a distinction on whether or not we use the dollar appropriation or foreign currency appropriation, and whether or not we treat it as a grant mechanism, or a contract mechanism that extends the intramural program. But in terms of the availability of foreign currencies, we have adopted, as a matter of practice, the policy of not sending dollars abroad if the Government owns foreign currencies in the country where the research is being supported.

Dr. ENDICOTT. Mr. Laird, I believe I can explain this particular paragraph. And it does not relate to foreign currency or Public Law 480 funds at all.

This relates to a problem which we began to encounter about 2 years ago, and there was quite extensive testimony last year by Dr. Shannon, I believe. We discovered that in the countries, and this instance in Western Europe, in which the medical research program is essentially under government control and financed by government in most instances, even though it may be carried out in universities, we were in effect, by making rather large grants to individual investigators without consulting the Government, upsetting substantially the plans of that Government for its overall development of medical research in that country. We therefore established some mehcanisms, for example, in Great Britain, whereby we make no grant to a university investigator or to an investigator in the medical research council apparatus without prior clearance with the University Grants Committee of England, or with the British Medical Research Council.

That is what this is talking about.

Mr. Laird. Well I really would like that cleared up just a little bit. The statement in the justifications book seems to imply that this procedure applies all the way through the National Institutes of Health.

Dr. Endicott. That is true.

Mr. Laird. The emphasis, I thought, was being placed in just the opposite direction.

Dr. Endicott. I think this probably got put in the wrong place. Because this is an arrangement, not with foreign currencies, but with hard currencies, and it relates to arrangements which we have made. And there is quite an elaborate clearance procedure for grants from certain countries before we even review them. I am sure that is what is being spoken about here.

And it seems to be under—that is the foreign currencies. It is in the wrong place.

GRANTS TO THE SLOAN-KETTERING AND OTHER INSTITUTES

Mr. Laird. I wonder if you could give me an idea of how much the National Cancer Institute is making available to the Sloan-Kettering Institute for cancer research?

Dr. Endicott. I could do that for the record. I do not have it with me, sir.

Mr. Laird. Then perhaps as long as you would be supplying that for the record, you could supply how much is made available to the Sloan-Kettering Institute out of all appropriations made to the Public Health Service?

Dr. Endicott. Yes, sir; I could get that information.

(The requested information follows:)

Support to Sloan-Kettering Institute

The National Cancer Institute is currently making available to the Sloan-Kettering Institute, for cancer research, approximately $1,828,740 in research grants, $174,935 in training grants, $1,826,000 in chemotherapy contracts, and $11,546 in fellowship awards to individuals sponsored by personnel on the staff of the Sloan-Kettering Institute. The Heart Institute is currently making available $109,183 in research grants.

Mr. Laird. This list of the largest grants that were awarded by the National Cancer Institute from 1956 to 1960, it seems to me, is prepared on the basis of grants to investigators rather than institutions. Is that correct?

Dr. Endicott. That is correct.

Mr. LAIRD. So that this does not in any way give a complete picture on the amount of funds that are going to each one of the institutions listed in this table?

Dr. ENDICOTT. In one instance it does, and in the other instances it does not.

Mr. KELLY. It was not intended to. It was intended to identify large project grants and not a summary of activity with an institution.

Dr. ENDICOTT. There is one here to Dr. Farber, to the Children's Cancer Research Foundation. It is essentially, it is not quite, but it is almost, our entire support to that institution.

In the case of the Sloan-Kettering grants that is not true.

Mr. LAIRD. You make a grant to Dr. Farber for $768,388. Is that an institutional grant?

Dr. ENDICOTT. No, sir. It probably compares to perhaps two of the grants at the Sloan-Kettering Institute, the one which covers clinical chemotherapy and basic chemotherapy research.

In the Children's Cancer Research Foundation there is a large program of drug development and drug testing which is all under the very close direction of Dr. Farber. It is a highly integrated organized program in which one senior investigator manages the entire operation.

In the Sloan-Kettering Institute this is divided among several different divisions with several different senior investigators managing different parts. Here we made divisional grants.

This was discussed yesterday by Dr. Shannon and was a specific example which he gave of the divisional grants. These are not institutional grants.

INSTITUTIONAL GRANTS

Mr. LAIRD. I did not mean in all of them. I was referring specifically to that one. It looked to me as if that, perhaps, came very close to being an institutional grant.

Dr. ENDICOTT. Well, it is an institutional grant in the sense that Dr. Farber is an institution. But there are many unrelated programs going on in the Children's Cancer Research Foundation which are not supported by this grant, and which we would not believe appropriate to be supported by this grant.

For example, the very important work on measles vaccine which is going on under the work of Dr. Enders.

Mr. LAIRD. Of course under an institutional grant you would not necessarily have to include that?

Dr. ENDICOTT. If you made an institutional grant for cancer research, you would probably not include it. The institutional grant, though, that has been presented and is proposed for activation would permit cancer, measles research or any medical research program.

Mr. LAIRD. So you would not anticipate that an institutional grant would be made to the Children's Cancer Research Foundation?

Dr. ENDICOTT. I think it might, sir, although the plan for the first year is to include only medical schools, dental schools, schools of osteopathy and public health. And in subsequent years, as I understand it, the plan is to extend the program to other institutions which have significant research operations, perhaps with a research budget over $100,000.

Dr. Farber's institution would clearly qualify.

QUESTION OF ADDITIONAL COST

Mr. LAIRD. In the discussion with the chairman of the committee a few moments ago, you indicated that if the institutional grants are not approved for 1961 you will have an unused appropriation which will revert to the Treasury?

Dr. ENDICOTT. This projection is very difficult to make, and I was intending to comment on it and did not earlier when we were talking about projected amounts for project grants.

Now I want you to understand why it is difficult to make this projection. There is not very much difference between a large project and a center grant. I suppose one might almost describe this grant to Dr. Farber as a clinical center grant. Now we have received applications this year in several different stacks, and one is called project grants and another is called the center grants.

We have not completed the review of our center grant applications. I do not know how much of that will be financable under the center grant appropriation, but all of it clearly could be financed as a project grant.

Now those figures, for the purposes of this projection, have not been included in the tables. And there are really only two Institutes that are far enough along in the center business even to have a large number of applications.

I do not know what the backlog in center grants is likely to be this year or next year. We have not reviewed any yet. I do not know what the percentage of approval will be, or how the financial picture will look. So this figure could be quite a way off.

Mr. KELLY. We probably erred in not explaining the basis of our projected backlog. We have allocated for the purpose of this table the moneys which were identified in the appropriations last year for each of the new special programs on the assumption that that precise amount would be used; and then dealt with research projects on the basis of the action of the study sections on the remaining grant funds.

Dr. ENDICOTT. We have had no experience.

Mr. KELLY. It had to have a series of assumptions in it. But we did fail to spell out that assumption as being the basis of this table.

Mr. LAIRD. On the basis of that table, one would be led to believe that the institutional grants do cost the Federal Treasury some additional money.

Mr. KELLY. As I explained yesterday, I think that you can come to no other conclusion with respect to 1961 or 1962. If you give the institutional grants a priority treatment, which was the concept of the legislation, within any given amount of money, you do not spend any more money than was provided; but you spend it for this purpose rather than for another purpose. If you did not make the institutional grant at all, and had not received applications equal to the amount of money allocated for the purpose, of course you would save some or all of the amount set aside for institutional grants.

On the other hand, if you spent it for institutional grants, you would be spending money in excess of what you would otherwise spend.

DIFFERENT TYPES OF GRANTS

Mr. LAIRD. Well now, you take this grant to the Children's Cancer Research Foundation in Boston. It would seem to me that that particular grant could fit into several definitions that are available to you at this time.

Dr. ENDICOTT. Yes, sir, it could.

Mr. LAIRD. In this same grant you are also making available a clinical center, aren't you?

Dr. ENDICOTT. No. We are providing support for clinical investigation which, in part, defrays research costs——

Mr. LAIRD. That also is tied to this project, is it not?

Dr. ENDICOTT. Yes, sir. But Dr. Farber has not had a geographically defined research ward as we have defined it in the general metabolic centers. He has taken care of patients scattered around through Children's Hospital. The foundation does not have a hospital of its own. There is not a single bed in the Jimmy Building.

Mr. LAIRD. Well, I am using this merely as an example to try to understand the definition of these various grants that you have, and it seems to me that different types of grants can cover the same areas in some instances.

Dr. ENDICOTT. Yes, sir; they can.

Mr. LAIRD. There is no clear-cut definition of these different types of programs which are eligible for funding.

Dr. ENDICOTT. No, sir; there is not. I think this is as confused an area at this moment as any that I can recall. And I sat yesterday and listened to the testimony, and was acutely aware of the difficulty of those of us on this side of the table trying to make those of you on that side of the table understand what we were talking about when we were not quite sure ourselves.

Mr. LAIRD. Is this because it is moving too fast, or what is the problem or reason we have not been able to get clear-cut definitions?

Dr. ENDICOTT. Well, sir, I do not know all of the answers. But I think various people have been trying to solve the same group of problems in somewhat different ways. In part the research professorship which was developed as a result of congressional action is an attempt to stabilize research careers. The institutional grant program, which is an administration proposal, has, as one of its major objectives, the same thing. It is quite clear that at least some of the staff involved in the center's grant can look forward to a stable career because these funds are envisaged as essentially permanent resources for the permanent Director.

We are in some ways trying to accomplish the same thing here with at least three different mechanisms. And if I strain perhaps I can think of one or two others. They are by no means discrete, separate, unrelated programs.

RESPONSIBILITY OF CHIEF INVESTIGATOR UNDER GRANTS

Mr. LAIRD. How much can one investigator handle, not only in the terms of his own workload, but also in terms of supervision? It seems to me that you have a problem here when you get into such a big individual grant. And I had envisioned this as an institutional grant. It just seems to me that you cannot hold an individual investigator responsible for $768,388.

Dr. Endicott. Well, that size of grant is about the same as some of the others on the list here. Now obviously there has to be substantial delegation of authority and responsibility for segments of the program in any operation of this size, just as there is in the intramural operation of the National Cancer Institute, which is quite a bit larger than that, and for which I hold Dr. Gordon Zubrod directly responsible.

But backing him up are a whole series of branch chiefs, laboratory chiefs, section chiefs, clinical directors, and so on. Now it depends a great deal on what kind of research you are doing as to how much on man can really give immediate scientific direction to.

Mr. Laird. That is the purpose of the individual grant, isn't it? Back of it was the idea that instead of giving it to the institution, we would give it to the investigator so that he would be responsible to the National Institutes of Health, and the National Institutes of Health would be responsible to the administration and to the Congress. I am not trying to pick on this one grant, but am just using it as an example. When I saw this list it made me think that this must be an institutional grant that we had already in existence.

Dr. Endicott. Now I very deliberately mention that it is important to recognize which field it is in because that happens to be a field in which much of the work is repetitive and routine and carried out by technicians. This has a very large component of drug screening in it. What you do in drug screening is the same old thing, day after day after day, using the same number of animals, using the same routine. The only thing that you change is the chemical that you inject, make the same measurements and same observations. And most of this is done by highly trained technicians.

Well, one good scientist can oversee a relatively enormous screening program.

Now we operate centrally from Washington a screening program which tests about 50,000 materials a year and 200,000-some-odd tests. And I rely for the quality of that screening program on one man who, although he has a staff, and operations scattered all over this country, is capable of detecting when this system is going sour and getting out there within 24 hours and fixing it. Now his program, I suppose, amounts to $5 million a year.

Now Dr. Farber has some very substantial elements of screening. And another area which costs a lot of money, as we were saying earlier, is therapeutic trial. Now if you took the screening component out of here, and the therapeutic trial out of here, this would be a much smaller grant. About all it would support would be some synthesis of chemicals which is relatively inexpensive. Now if this were fundamental biochemistry it would be preposterous to ask one biochemist to give very close guidance to a program of $700,000.

DEFINITION OF INDIVIDUAL AND INSTITUTIONAL GRANTS

Mr. Laird. I understand what the program is, but what I am still trying to get at are these definitions. At some place in the record I would like to have a definition of institutional grant and a definition of a grant to an individual investigator, and just how these differ.

You can supply that for the record.

Dr. ENDICOTT. Yes, sir. Perhaps Dr. Shannon would like to supply that.

(The information requested follows:)

DEFINITIONS OF GRANTS INCLUDED UNDER "RESEARCH" IN THE NIH APPROPRIATIONS

The appropriation activity "Grants: Research" includes funds for the support of project grants, center grants, and institutional grants. The definitions used by the National Institutes of Health are not mutually exclusive, but serve as general guidelines to identify these grants as follows:

I. THE PROJECT GRANT

The project grant includes projects ranging from the traditional, discrete, and specifically detailed type of research activity to the broadly based type of search project commonly identified as program projects.

A. The project grant

The traditional project grant is an award to an institution in the name of one or more individual investigators for a discrete, specified, circumscribed project to be performed by the named investigator(s) and representing his specific interest and competence. Normally only one department, or segment of a department, is involved and the amount of money awarded is usually not large.

B. The program project grant

A grant for a research program project is an award made to an institution, in the name of one or more principal investigators, for the support of a broadly based and usually long-term program of research activity. Program projects are flexible in nature, ordinarily require large sums of money, and typically involve the efforts of entire departments or divisions of institutions. They are usually directed toward a range of problems within a broad category rather than toward a specific single-purpose investigation. Frequently, a program project grant results from the combining of a series of individual projects of the traditional type.

Program project grants include certain types of activities which, in the developmental stages, have been described as centers. These include categorical centers, clinical centers, and aging centers. Grants for this type of activitiy will be included as program project grants. The only grants which will continue to be called center grants are described in section II.

II. THE CENTER GRANT

The center grant is an award made to an institution to provide the basic physical resources and the support of common services for broad and flexible research efforts, such as an integrated system of resources and services essential to the conduct of clinically oriented research by an institution. Center grants are generally provided for noncategorical research resources. However, it is contemplated that categorically oriented projects may develop which require discrete facilities. Operating expenses for the substance of the research program to be carried out in the research center generally are not provided as part of these awards. Substantive support is normally provided through program project grants. Research center grants are made to a duly constituted organization, or a unit thereof, in the name of an appointed director who is responsible for the administration of the center and its staff.

III. THE INSTITUTIONAL RESEARCH GRANT

The institutional research grant is an award made to an institution for the general support of research and research training programs of the institution under conditions which give the institution a latitude of flexibility and freedom of decision in determining the specific purpose for which these funds will be used. The awards are to be made on a formula basis, by class of institution, rather than on the basis of considering specifically prescribed projects, programs, or areas of research.

Among the kinds of urgent research needs for which an institution may choose to use its institutional research grant funds are:

A. Research resources of a general nature which are essential for all research programs but are not properly allocated to any particular project or program, e.g., facilities for experimental animals.

B. Funds for small, pilot, and exploratory studies to determine whether formal requests for longer term support are warranted.

C. Emergency funds for unanticipated needs for research supplies, equipment, or personnel.

D. Funds to permit the institution to provide more stable positions and salaries for senior scientists now working under the tenuous support of the project system.

GRANTS FOR MEDICAL RESEARCH FACILITIES UNDER 433(a)

Mr. Laird. I note in your statement where you talk about the grants for construction on a nonmatching basis, that you have referred to these grants in the same manner that Dr. Shannon did yesterday You add the qualifying statement: "Which was authorized for 1 year." Why didn't you say that where you are talking about some of these other appropriations? It seems to me there is no difference between that appropriation and any other appropriation in your budget. Why did you pick that out, and make that qualifying statement?

Dr. Endicott. Well, sir, it was my understanding that this had been singled out specifically as a program which was limited to 1 year. This was the understanding which I had at the time we prepared our first budget estimate.

Mr. Laird. Well, this legislation that the Public Health Service and the Administration has before Congress to repeal section 433(a) of the Public Health Service Act has not been passed by the Congress as yet.

Dr. Endicott. No, sir.

Mr. Laird. I realize that there has been such a recommendation made, but there really has been no action by the Congress. I have had an opportunity within the last 24 hours to talk to various members of the legislative committee, and I really do not think you have much assurance that you are going to get that repeal.

NEED FOR CONSTRUCTION OF FACILITIES

What do you think of the need for medical research facilities? How great is this need? You made a study of this even before you were made Director of the National Cancer Institute, isn't that correct?

Dr. Endicott.. Yes, sir.

Mr. Laird. There is probably no witness who is better qualified than you to give a professional judgment as to the need for research facilities. I would like you to give me your personal views as to the need for research facilities. I do not want you to be bound by the recommendation of the administration as you answer this question. I am asking you this as an individual who has made a study of research facilities throughout the United States.

Dr. Endicott. Well, it is my impression that although the present matching program has accomplished tremendous good, and that there is a continuing splendid opportunity to accomplish good by such a program, and that many of the needs for research today will ultimately be satisfied by such a program, that it does not work well in certain situations, certain geographical areas, certain institutions.

One of the major limiting factors for cancer research for some time has been facilities. Dr. Shannon mentioned several examples yesterday. Early in the chemotherapy program I nearly went out of my mind trying to meet the problem of mouse supply because you cannot breed inbred mice just anywhere. You need quite a special facility. And I had no way to get them built. And the concerns that I had to turn to, who were competent, would not have qualified under the grant program.

They were commercial laboratories, and they were going to undertake this under a contract. Now this is a limited example, but it is an excellent one for any institution which is tackling target research programs. If the Government wants a building built in order to carry out a project that the Government wants done, and it is not one that the other institution is coming to sell the Government, it is pretty hard to go out and get them to put up matching money for a building in which to do it.

So this is one area where a matching program does not do the job.

Then the primate center, the way in which we are operating the primate center program, is a recognition of that fact. It is unreasonable to expect a single university to raise matching funds to build a facility which will serve an entire region, and perhaps half of which will be reserved for investigators from other institutions. So that is one general type of problem.

Another obvious one relates to institutions that are either in economically depressed areas or are impoverished institutions even though they may be in an area of economic plenty, and which they cannot get started in research because they do not have many investigators, and they cannot get any investigators because they do not have any building, and they cannot get either one because they do not have any money and they just cannot make a start.

And it is not a question of matching, they do not have any money to start anywhere.

Now other institutions have made a start, but they have so many demands on their limited number of dollars that they simply cannot get matching money. Now in the studies which I made, which were very hurried, we had no opportunity to really assess the extent of this problem. I could not give you any report that relates to dollars, but I am sure that there are many situations where many institutions, for some time to come at least, will not be able to meet their building needs if matching is required.

Now this is, as Dr. Shannon said, a big problem, a problem of national policy. It is a question of general needs versus specific needs. There are many needs which will be met—have been met—by matching programs. There are others which may never be met that way or, if they are, it is some considerable time in the future.

APPLICATIONS FOR GRANTS FOR CANCER RESEARCH FACILITIES

Mr. Laird. In the area of cancer research facilities, limited to this categorical area, you have before you at the present time, I understand, a group of applications for medical research facilities. One of the requirements of these applications was the certification that all avenues had been investigated and that the facility which was proposed could not possibly be constructed if they were required to meet the standards of the Medical Research Facility Act. What do these applications total in dollars and cents?

Dr. Endicott. We have before us for consideration at the next meeting of the Council some 30 applications for $25,819,165.

Mr. Laird. And there is a certification with these applications that the research facilities could not be constructed under any other program?

Dr. Endicott. We have asked them to demonstrate that they have exhausted every reasonable possibility of raising matching funds. Now, of course, all of these applicants will be visited before their grants are acted upon. The visiting teams are now in the field. The Council meeting will be at the end of April, the 29th and 30th of April and 1st of May.

I had had an opportunity to talk to the site visitors, who have visited perhaps half by now, and the report was made at the Council meeting a week or so ago, 2 weeks ago I guess it was, that none of the applicants visited at that time could be excluded from eligibility on this basis. In other words, so far as the visitors could tell, they had, in fact, exhausted every reasonable possibility of raising matching funds.

Mr. Laird. Personnel was available under each of these applications to carry on the research that they planned?

Dr. Endicott. I would have to give an "iffy" answer there. This was not part of the question that I put to them. But I would assume so, knowing the institutions.

Mr. Laird. But isn't it true that that is set forth in their applications?

Dr. Endicott. Yes. Oh, yes; of course.

Mr. Laird. But you did not happen to ask that question of the people that had made the site visits; is that correct?

Dr. Endicott. That is correct.

Mr. Laird. But in the application, they have to show that they have the investigators to do the work that they propose in the new facility.

Dr. Endicott. Yes, sir.

Mr. Laird. You have $5 worth of applications for every $1 that you have available to you for this program.

Dr. Endicott. Yes, sir.

Mr. Laird. Do you know of any other program in the National Cancer Institute where there is such a great demand for funds, in any ratio like that?

Dr. Endicott. Not this year, sir.

RECOMMENDED REPEAL OF SECTION 433(a)

Mr. Laird. Were you asked for a recommendation as to whether section 433(a) should be repealed?

Dr. Endicott. No, sir; I was not.

Mr. Laird. And you are one of the administrators that is presently using this particular authority, or will be using it in this fiscal year?

Dr. Endicott. Yes, sir.

Mr. Laird. It seems to me you are the only one?

Dr. Endicott. No, sir. I believe Dr. Watt also——

Mr. Laird. I thought he used it in fiscal year 1960?

Dr. Endicott. I am not sure about this.

Dr. Watt. Also this year.

Mr. Laird. I did not realize you were using it for grants this year. But this was never discussed with you before this recommendation was sent up to the Hill?

Dr. Endicott. Well, sir, I have many discussions of construction problems and construction legislation with Dr. Shannon——

Mr. Laird. I am not trying to put you on the spot, but was the recommendation submitted to you for comment?

Dr. Endicott. No, sir. This would not ordinarily be done. Recommendations for legislative amendments ordinarily originate at the bureau level and proceed upward, not downward. So there is nothing unusual about this. As a matter of fact, they often originate much higher in the——

Mr. Laird. I would think there would at least be some consultation with the program people. I am surprised to learn that there is no consultation with the program people in an area so important.

Dr. Endicott. I do not think you can say there has been no consultation. There have been extensive discussions at every level on the problems of construction, and I am quite sure that Dr. Shannon does not need to consult with me on something like this to know my views, nor, indeed, with the other Institute directors.

Mr. Laird. I do not take it that it is your personal view, from what you said here today, that we should repeal section 433(a)?

Dr. Endicott. I would like to give a qualified answer to that if I might. If the general program were adequate, I think there would be no need for——

Mr. Laird. I will put it this way to you: The recommendation to the Congress is a 50–50 matching program at $50 million and repeal of section 433(a). Would you be in favor of repealing that section on that basis?

Dr. Endicott. Well, not violently in favor of it, sir.

Mr. Fogarty. That is a pretty good answer. I'm sure we understand you.

Mr. Laird. That is all I have, Mr. Chairman. The hour is late.

Mr. Fogarty. Do you have anything else you would like to say, Doctor?

Dr. Endicott. No, sir.

Mr. Fogarty. Thank you very much.

Incidence and Cost of Cancer

We shall place your statement on incidence and cost, and the highlights statement in the record at this point.

(The statement referred to follows:)

Incidence and Cost of Cancer

Public Health Service National Cancer Institute

Statistics of the annual number of deaths and total current number of disabilities caused by the major diseases dealt with in the National Cancer Institute, and the estimated annual cost to the Nation.

I. Cancer deaths in 1959 (unpublished data supplied by the National Office of Vital Statistics):

Buccal cavity and pharynx	6,053
Digestive system	89,490
Respiratory system	37,413
Breast	23,085
Genital organs	39,109
Urinary organs	12,493
Other sites	28,663
Leukemia	12,270
Lymphomas	12,471
Total, all sites	261,047

II. Cancer disability in 1959 (estimated on the basis of data supplied by the National Cancer Institute and the National Health Survey).

(*a*) Estimated cases under treatment, 782,000.

(*b*) Estimated person-days of disability (these estimates have a large margin of error): 1. Restricted activity, 37.9 million; 2. sick in bed, 22.5 million.

III. Cancer's cost to the Nation in 1959:

(*a*) Hospital bill, $350 million (estimated by the American Cancer Society).

(*b*) Loss of income, $91 million (estimated by assuming that 1 in 7 person-days of restricted activity represents a lost working day, that there are 250 working days in a year and that an average annual income is $4,200). This must be considered a minimal estimate. Not included in this estimate is the loss of productivity due to retirement for cancer disability nor the loss of potential productivity because of a cancer death during the working years.

(*c*) Estimates based on the average annual contribution per member of the labor force (age 18 to 65) to the gross national product indicate that cancer brings about a loss to society in goods and services valued at approximately $15 billion per year.

HIGHLIGHTS OF PROGRESS IN RESEARCH ON CANCER, 1960

Items of Interest on Program Developments and Research Studies Conducted and Supported by the National Cancer Institute

The National Cancer Institute gave increasing emphasis to development and expansion of programs especially oriented to research on human cancer. At the same time, laboratory, clinical, and field studies contributed to the accumulation of knowledge necessary for a more complete understanding of malignant disease.

The Institute invested over $5 million in virus-cancer research grants. One such grant-supported study reported the discovery of a filterable agent that induced immunity in rats to six different tumors. This discovery reemphasized the complex interrelationships that may exist between infectious disease and resistance or susceptibility to tumor development. Environmental studies in several States confirmed earlier reports of the higher incidence of cancer among urban compared with rural residents. Information such as this may lead to better understanding of the causes and, subsequently, more effective ways for preventing some kinds of cancer.

The Cancer Chemotherapy National Service Center is now sponsoring clinical trials of more than 150 drugs. One investigation reported successful use of a new hormonelike compound, delta-one-testololactone, in temporarily controlling, with no masculinizing side effects, the lesions resulting from the spread of breast cancer. A comprehensive review of meningeal leukemia suggested a treatment method. Other data on advanced refractory acute leukemia provided detailed new information on the natural history of this form of cancer.

The items presented in this report are representative of the highlights of program developments and progress in research conducted and supported by the National Cancer Institute. Institute staff scientists are identified by the laboratory or branch with which they are connected and grantees by their institution. Most of the results were reported by groups of investigators, but for the sake of brevity, only the senior author is identified in most of the summaries.

VIRUS RESEARCH

Further studies describe tumors in mice receiving polyoma virus inoculation

The SE polyoma virus has become an important laboratory tool in the intensified research now underway to learn whether viruses cause human cancer. Dr. Sarah E. Stewart, Laboratory of Biology, and Dr. Bernice E. Eddy, Laboratory of Viral Products, Division of Biologics Standards, have reported extensively on their collaborative studies of the virus, which Dr. Stewart obtained from the tissues of leukemic mice.

Further studies on the development of tumors in mice inoculated with polyoma virus have been reported by Dr. Mearl F. Stanton, Laboratory of Pathology, and Drs. Stewart and Eddy. Swiss mice inoculated late in fetal life with tissue culture preparations of the virus developed a greater incidence of tumors and died earlier than mice injected shortly after birth. However, no type of tumor was found that had not been previously observed in mice inoculated as newborns.

Mice inoculated as newborns from mothers exposed to an environment contaminated by the virus had a significantly longer lifespan and lower incidence of salivary-gland tumors than mice inoculated as fetuses in contaminated mothers or as newborns from uncontaminated mothers.

Mouse maternal antibodies in milk and serum induce polyoma virus resistance

Drs. Stewart and Eddy reported that the resistance which mice develop to tumor induction by the SE polyoma virus was traced to the presence of maternal antibodies in milk and serum.

Milk taken from nursing mothers that had been exposed to the virus and from those not exposed showed pronounced differences in antibody titers. Mice of the maternal strain that were housed in the same room with mice that had received polyoma virus had serum antibodies specific for the virus. Pooled sera from 12 breeders completely inhibited tumor induction in 24 mice given sufficient virus to cause tumors in all of 16 mice that did not receive serum.

The range of antibody titers of pooled milk from exposed mice, as shown by tests on the inhibition of hemagglutination of guinea pig red blood cells, was similar to that observed in the sera of exposed mice.

No correlation observed between polyoma antibody and leukemia in mice

Dr. Lloyd W. Law, Laboratory of Biology, has collaborated with scientists of the National Institute of Allergy and Infectious Diseases, in a study of the relation of polyoma virus infection to lymphocytic neoplasms in mice.

Leukemic and nonleukemic mice of four high leukemic strains were tested at intervals for antibody to polyoma virus. No correlation was found between the presence of detectable antibody and the appearance of leukemia at various times throughout life. No evidence was observed that mice with circulating antibody against polyoma had an increased risk of developing leukemia. The relationship between antibody status and recovery of virus from organs of leukemic mice was found to be similar to that previously observed in nonleukemic mice of infected colonies by Dr. Wallace P. Rowe, National Institute of Allergy and Infectious Diseases, and others.

The results suggest that any association of polyoma virus and experimental transmission of leukemia is fortuitous.

Study confirms lodging of polyoma virus chiefly in infected cell nuclei

Dr. Richard A. Malmgren, Pathologic Anatomy Branch, has reported results of a study strongly suggesting that the polyoma virus localizes primarily in the nucleus of infected cells.

Polyoma virus was grown in cultures of milk-adapted mouse lymphoma cells. The infected cells were exposed to labeled antipolyoma virus serums. These had been obtained from rabbits immunized against the virus and had been labeled with fluorescein isothiocyanate. The cells were fixed on slides and examined under ultraviolet light. Clumps of fluorescent material of varying size were scattered throughout the nucleus and were particularly prominent near the inner surface of the nuclear membrane. These fluorescent particles were not see in uninfected tissue-culture preparations.

Since the deposition of dye-labeled antivirus serums is dependent on an antigen-antibody combination, the finding is interpreted as demonstrating either virus or virus-associated antigen in the nucleus of cells infected with polyoma virus.

Cytochemical studies reported by other National Cancer Institute investigators have demonstrated abnormal nucleoprotein in vacuoles within the nucleus of polyoma virus-infected cells. The present finding is consistent with these observations.

Electron microscope studies at the National Cancer Institute have also demonstrated large collections of viral particles within the nucleus of infected mouse lymphoma cells. However, the electron microscope studies also showed viral particles in the cytoplasm of infected cells. It is suggested that the concentration of viral particles in the cytoplasm may be too small to be revealed by the fluorescent antibody technique.

Rous virus pinpointed in sarcoma cell cytoplasm

Dr. Malmgren and his associates in other laboratories of the National Cancer Institute have also reported results of a study designed to pinpoint the location of the Rous sarcoma virus within the cells of the Rous sarcoma. Electron microscope studies previously reported in the scientific literature demonstrated particles thought to be the Rous sarcoma virus in the cytoplasm of sarcoma cells.

Chicken and turkey anti-Rous sarcoma virus serums obtained from fowl in which Rous sarcomas had regressed were labeled with fluorescein isothiocyanate. When sections of sarcoma tissue were exposed to the fluorescein-labeled anti-Rous virus serums, fluorescence was observed in the majority of instances in the cytoplasm of sarcoma cells. Occasionally, intranuclear fluorescence was noted. The number of sarcoma cells containing the fluorescent material was related to the amount of virus inoculated into chickens to initiate tumors.

Fluorescence was not seen in the cells of normal chicken tissues exposed to the labeled anti-Rous sarcoma virus serums.

Tissue culture technique for assay of tumor virus developed in grant study

A possible new tool for approaching the problem of studying viruses as causative agents in cancer is suggested by recent findings in in vitro studies of the chick embryo—Rous sarcoma virus (RSV) system. Dr. Harry Rubin, University of California, Berkeley, reported that the studies pointed the way to the use of RSV for assaying lymphomatosis virus, which does not produce overt cytopathic effect in vitro, in cultures of chick embryo cells.

The study had its origin in the observation that resistance to infection with RSV occurred sometimes in chick embryo cultures. The resistance was found to be associated with the presence of one or more embryos whose cells were found to be resistant when cultivated separately.

An agent, named resistance-inducing factor (RIF), was isolated from the medium of resistance cultures. RIF multiplied extensively in infected cultures and could be measured quantitatively. It was sedimented in the ultracentrifuge under conditions adequate to sediment RSV, and could be neutralized by antiserum to RSV (obtained from chickens that had recovered from tumors induced with RSV).

These characteristics, as well as the widespread occurrence of RIF in eggs, suggested that RIF is a virus of the avian lymphomatosis complex. Support for the latter relationship was found in the observation that four strains of lymphomatosis virus mimicked the action of RIF by inducing resistance to RSV in chick embryo cultures.

This finding led Dr. Rubin to suggest that the technique—in which one virus acts as a specific inhibitor of the growth of another—might be adapted to the detection of viruses associated with other malignancies.

A new filterable agent induces in rats immunity to six different tumors

A new method of inducing immunity against several widely employed transplantable rate tumors has been reported by Dr. Jerome H. Sacks and his colleagues at the Medical College of Virginia. The immunizing material, which was discovered in the investigators' laboratories, is an infectious replicating agent and produces in rats an acute hemolytic anemia.

At the time the report was prepared, this agent (FHA, filterable hemolytic anemia) had been transmitted serially in over 140 passages in some 2,500 rats and had remained stable both in its infectivity and the hemolytic syndrome it produced. The hemolytic disease is transmitted by inoculation of any of a variety of tissues or fluids taken from an animal at the height of the disease. For example, one one hundred-thousandth milliliter of serum administered intraperitoneally is sufficient to infect normal animals. FHA is strongly antigenic and stimulates the production of neutralizing antibodies. It is extremely small—filterable through filters with pore diameters of 20 millimicrons—and is nonsedimentable in the ultracentrifuge even under such drastic conditions as 144,000 g (units of gravitational pull) for 10 or 12 hours.

In the present study, 60 (54 percent) of 111 FHA-immune rats were resistant to transplantation of six different tumors; 7 (6 percent) of 114 control rats receiving transplants of the same tumors remained tumor-free. FHA-immune rats were those that had recovered from the hemolytic disease following intraperitoneal inoculation of infectious whole blood.

Some FHA-immune rats that developed tumors survived three times as long as the controls. In others, the tumor that developed was altered in growth pattern, gross appearance, and histologic morphology. The changes, never observed in control animals, included encapsulation without infiltration, extensive necrosis, and a more differentiated appearance. These results are interpreted as manifestations of heightened host resistance.

Additional evidence demonstrating the presence of humoral antibodies in animals recovered from infection with FHA was found in experiments in which tumor cells were incubated in the test tube with sera from FHA-immune animals. The sera were extremely toxic for the tumor cells, but not for normal cells present in the mixture. Control sera did not produce cytotoxic changes in either normal or tumor cells.

Dr. Sacks believes the findings suggest that the tumors studied share a common antigen with the FHA agent not possessed by normal rat tissues.

Moloney mouse leukemia virus studies summarized

Dr. John B. Moloney of the Laboratory of Biology, has reported a detailed study of a virus that induces lymphocytic leukemia in mice. His first report of the isolation of this virus from transplantable sarcoma 37 was made a year ago.

This virus is characterized by the following biological and physical properties: (1) infection by the agent is not limited to the very young or to mice of a single genetic type; (2) the virus-induced lymphocytic leukemia is similar to the sponstaneous type of the disease; no other neoplasms have been observed in the test mice regardless of strain used or age of the recipient at the time of virus inoculation; (3) the high tumor-producing activity of the virus concentrates induces leukemia in essentially 100 percent of the inoculated mice within a relatively short latent period—2.5 to 3 months; (4) as observed in the electron microscope, by Dr. A. J. Dalton, also of the Laboratory of Biology, the virus particles measure 65 to 100 millimicrons in diameter; and (5) the agent is stable to freezing and lyophilization.

The high biological activity, stability, and absence of strain specificity indicate that this virus may be a valuable addition to the group of tumor viruses now available for laboratory investigations.

Transplants of viral leukemia tissue induce solid tumors in mice

A "leukemia-like disease" in mice, induced by a virus and transmissible by cell-free filtrate, was described several years ago by Dr. Charlotte Friend at the Sloan-Kettering Institute for Cancer Research. The view of the neoplastic character of this disease was challenged on the grounds of inability to produce tumors by transplantation of leukemic cells. Drs. Rita F. Buffett and Jacob Furth, at the Children's Cancer Research Foundation, have now reported success in producing transplantable reticulum-cell sarcomas, originating from the systemic disease induced by the Friend virus.

The tumors arose in mice receiving subcutaneous or intramuscular grafts of liver fragments from animals infected with the virus. Tumor transplantation was facilitated by preirradiation of test animals.

The tumors grew locally, attained large sizes, and could cause death, with or without generalized leukemia. They closely resembled autonomous, supposedly virus-free reticulum-cell sarcomas. A number of the animals that developed tumors also had enlarged spleens characteristic of the generalized Friend leukemia, suggesting the presence of the virus in some of the tumor-bearing hosts.

Precancerous mammary tissues of mice show viruslike particles

The results of many electron microscope studies reported in the scientific literature have shown viruslike particles in tissues of mice known to carry the mammary-tumor virus. Yet, unequivocal proof of the identification of the particles with the biologically active virus is lacking. Dr. Dorothy R. Pitelka and her associates at the University of California, Berkeley, have now reported new evidence to support the theory that such particles are identical with the mammary-tumor virus.

Earlier studies in this laboratory had shown that viruslike particles were abundant in tumor tissue and hyperplastic alveolar nodules of C3H/Crgl mice, a strain that has a high incidence of mammary tumors, and that the hyperplasias were preneoplastic.

The present study has confirmed the consistent occurrence of these particles in hyperplastic mammary tissues of this mouse strain; it has shown the occurrence of these particles in hyperactive outgrowths of nodules transplanted into the glandfree mammary fat pads and in similar hyperplastic tissues from four C3H mice is established."

On the other hand, hyperplasias that are not preneoplastic, such as perlactating lobules of pregnancy, outgrowths from normal transplants, and "noduloids" induced by the administration of hormones, contained only rare, scattered particles.

The investigators conclude from these findings that "a clear and consistent association of viruslike particles with precancerous mammary hyperplasias in C3H mice is established."

Institute increases support of research on viruses and cancer

National Cancer Institute grants for research on the possible relationship of viruses to cancer, including cancer in man and experimental animals, totaled over $5 million during 1960. Many of the grantees are virologists who have recently turned to long-term cancer research.

At several meetings, members of the viruses and cancer panel of the National Advisory Cancer Council stressed the growing demand for research materials needed in the tremendously increased program of virus-cancer research. How to meet the first need—standardized cultures of living cells for the study of viruses suspected as cancer agents—has now been worked out. A national cell culture collection coordinating committee was established to develop criteria for certifying and preserving strains of mammalian cells of interest in cancer research. Well over a dozen laboratories in the United States are at present interested in assisting with this effort and the American type culture collection in Washington, D.C., is to serve as a repository and distribution center for such standard cell strains as are needed by investigators.

In order to meet another need of expanded virus-cancer research, the National Cancer Institute awarded a contract to the University of Kansas Medical Center to develop detection agents which will identify some of the many viruses found in the human digestive tract. The work of the Kansas Medical Center laboratories had previously been developed by National Foundation support in their polio studies. Other contracts for detection agents to identify other groups of viruses are expected to be awarded in the future. This is a vital first step necessary before determination of any causal relationship between these viruses and cancer in man.

Additional needs of virus-cancer investigators which members of the viruses and cancer panel hope will be met with the assistance of the National Cancer Institute include: (1) development of a laboratory animal (probably the mouse) whose viruses and genetic characteristics are known; (2) detection agents for identifying viruses present in such animals; (3) increased availability of monkeys and other primates for studies of human viruses suspected of causing cancer; (4) provision and distribution of an adequate supply of human normal and malignant tissue and blood; and (5) design and production of special research equipment, such as a liquid nitrogen refrigerator for indefinite preservation of living cells at extremely low temperatures.

Summer institutes for scientists in fields related to virus research and more extensive use of present training programs have been suggested as ways of stimulating interest in the virus-cancer field and enlarging the number of trained investigators. Distribution of translations of foreign scientific papers and more special symposiums on current problems will help to meet a recognized need for improvement in communication in the fast-moving area of cancer virology.

ENVIRONMENTAL CANCER

New York State cancer incidence pattern same as for Iowa, Connecticut

Scientists of the New York State Department of Health and the National Cancer Institute have collaborated in an epidemiological survey of cancer incidence in urban and rural areas of New York. The data, reported by Dr. Morton L.

Levin, now at the Roswell Park Memorial Institute, and William Haenszel, Biometry Branch, National Cancer Institute, were obtained for the period 1949–51 from a central cancer register maintained by the department of health. All physicians, hospitals, and laboratories in the State (exclusive of New York City) report cancer patients to this register.

The cancer risk was generally greater for the urban than for the rural population. Urban-rural ratios of incidence rates were higher for males than females. The largest urban-rural ratios noted for males were for the respiratory system, buccal cavity, and pharynx, esophagus, intestine, rectum, and urinary organs; for females, buccal cavity and pharynx, and urinary organs. The findings showed substantial agreement with the incidence rates and urban-rural ratios of rates reported from Connecticut and Iowa.

Cancer mortality rate among nuns and women in general compared

Previous studies have suggested that women in religious orders have a higher risk of developing cancer of the breast and a lower risk for cancer of the uterine cervix than other women. Dr. Ruth S. Taylor and her associates in the Field Investigations and Demonstrations Branch, have now reported results of a study comparing mortality among three orders of Roman Catholic nuns with that of a group of women in the general population of similar age and background, with particular reference to cancer. The study was designed to detect any differences that might be attributed to the single as contrasted to the married state, and to obtain definitive information concerning total cancer and some of the major causes of death other than cancer.

The findings of the present study with respect to breast cancer are in general agreement with those of previous studies, all of which indicate that single women have a lower risk of mortality from breast cancer early in life, then increasingly higher rates, with a lifetime rate that is much higher than that of married women.

The results also confirmed a mortality risk for cancer of the uterus that is much higher among married than among single women. The evidence indicates that the difference is due to a deficiency in the rate of cancer of the uterine cervix among single women.

The sisters showed lower total cancer mortality than did the controls between the ages of 20 and 59, higher rates above that age, and total experience about the same. They showed a much higher mortality rate from tuberculosis than did the controls, the highest risk occurring between the ages of 20 and 29. In mortality from cardiovascular-renal disease the sisters had more favorable experience than did the controls, particularly after age 50.

Cigarette smoke may play physical, not chemical role in cancer of lung

Dr. Paul Kotin at the University of Southern California School of Medicine, Los Angeles, has published a report on the role of cigarette smoking in the development of lung cancer.

Laboratory analysis was made of the content of aromatic polycyclic hydrocarbons in the mainstream smoke, which consists of aerosols respired by the smoker, and in sidestream smoke, which represents the smoke from the burning end of the cigarette.

The 3,4-benzpyrene content was of particular interest because it is a well-known carcinogen (cancer-causing substance) for animals and is present in considerable quantity in cigarette smoke. The carcinogen was detected in the condensate collected in 8 puffs as follows: mainstream smoke, 35 to 50 micrograms per cigarette; sidestream smoke, 135 micrograms per cigarette. There was, thus, greater production of the carcinogen during the period between puffs than during the time of actual smoke inhalation.

Other laboratory studies were conducted to determine the effect of cigarette smoke on the physiological activity of the respiratory epithelium. Isolated epithelial segments were exposed to aerosols containing cigarette smoke products in a specially designed chamber. Three phases of response were observed in the flow of mucus on the epithelium: first a sharp increase, which reached a peak in a few seconds, then a sharp decrease of about 16 minutes' duration, and finally a recovery period of about 30 minutes' duration. When epithelium was exposed repetitively to simulate smoking conditions, the inhibition or slowing of mucous flow was intensified.

It was concluded that the data confirm results of numerous other laboratory and epidemiological studies showing that cigarette smoking is a causative factor in the increasing incidence of lung cancer. However, Dr. Kotin disagrees with the conclusion that it is the presence of certain carcinogenic hydrocarbons in the smoke which explains its role in the development of lung cancer. Rather, he suggests that cigarette smoke is a potent irritant of the tracheobronchial epithelium. The irritant effect is wholly unspecific and is capable of being produced by numerous other environmental irritants that differ from cigarette smoke both in chemical composition and physical properties. The adverse effect of cigarette smoke is produced by impairing ciliary action, slowing mucous flow, facilitating prolonged retention of particles, and increasing cellular permeability.

Dr. Kotin's work was supported in part by grants from the National Cancer Institute and the Division of General Medical Sciences. The paper is the second in a series on the relative etiological significance of several environmental factors that may be associated with the development of lung cancer. In the previous paper, the role and mechanism of action of air pollutants were discussed.

Further studies show chromium compounds are carcinogenic for mice

Dr. William W. Payne, of the Environmental Cancer Section, has reported further evidence of the carcinogenicity of chromium in laboratory animals. The results were obtained in a continuing study to learn whether chromium in one or more forms is responsible for the increased rate of lung cancer among chromate workers.

About a year ago, in collaboration with Dr. Wilhelm C. Hueper, head of the Environmental Cancer Section, Dr. Payne reported the development of cancers in rats that received implants of moderately soluble chromium compounds. The present study was undertaken to determine whether the compounds would produce similar results in another species, the mouse.

Mice receiving intramuscular implants of calcium chromate and sintered calcium chromate (prepared by heating pure calcium chromate to approximately 2000° F. for about an hour) developed tumors at the site of implantation. Sintered calcium chromate produced more tumors than did calcium chromate. The tumors, which began to appear 7 months after administration of the carcinogen, were sarcomas of the spindle cell or fibrosarcomatous types.

Dogs fed large quantities of an insecticide develop cancer of the gallbladder

The development of gallbladder and bile duct adenocarcinomas has been reported in dogs fed massive, toxic quantities of an insecticide, Aramite, over a long period. During a period of 46 months, 28 dogs received from 500 to 1,429 parts per million of Aramite per day. Fifteen of 19 animals autopsied after 462 to 1,220 days had one or more well-differentiated adenocarcinomas in the bile ducts and gallbladder. This effect was different from that in rats and mice, which develop liver damage and in some instances liver cancer.

Aramite, a mixture of two closely related organic sulfites, is a commercial insecticide, especially effective as a miticide, and is manufactured by the Naugatuck Chemical Co., a division of U.S. Rubber Co., Naugatuck, Conn. This material was undergoing a series of tests by the investigators who made the present report to determine whether residues of one part per million on certain food crops were safe for human consumption. The Federal Register of February 12, 1960 (vol. 2, p. 17, "Pesticide Regulations") lists the establishment of a zero tolerance for Aramite for a long list of fruit and vegetable crops.

The study was made collaboratively at the Memorial Center for Cancer and Allied Diseases, Mount Sinai Hospital, New York City; and Food and Drug Research Laboratories, Maspeth, N.Y. It was reported by Dr. Stephen S. Sternberg and his associates.

DIAGNOSTIC RESEARCH

Diagnostic research seeks procedures for detecting unsuspected, early cancer

Since early detection of cancer is of vital importance, the National Cancer Institute has in progress a program of intensive research in diagnosis, with the objective of devising procedures that will reveal the presence of unsuspected, early cancers. Established 2 years ago, the program employs a broad interdisciplinary approach and is being carried out through contractual arrangements, direct cooperative activities, and research grants.

As of October 15, 21 contracts in the amount of $1,019,000 and 68 research grants totaling $1,101,000 had been awarded to investigators working toward the development of a number of methods for detecting cancer in its early stages. These studies are based on the recognition of cancer as a group of diseases rather than a single disease and therefore look forward to the development of several diagnostic procedures.

Some of the new studies are concerned with correlating the presence of certain enzymes in the blood or urine of a patient with the existence of specific cancers. Other investigations are designed to determine the relationship between cancer and protein patterns observed in body fluids and secretions. Variations in hormone patterns between cancerous and noncancerous individuals are also under study.

Preliminary tabulation of the Institute's series of studies of vaginal specimens obtained from over 600,000 women and examined by the cytologic technique confirms earlier reports of the value of this method as a means of detecting early cancer of the uterine cervix in large population groups. Evaluation of the data should also produce information on the natural history of this form of cancer.

More than 3 million women each year receive cervical cancer examinations by the cytologic technique. A large percentage of them are obtained from personal physicians. It is believed that the systematic application of the cytological examination to the total female population followed by treatment as indicated could result in the virtual elimination of cancer of the cervix as a cause of death.

With this encouragement, investigators are intensifying their search for ways to adapt the cytologic method for the study of cancer of other body sites. Five of the 11 direct cooperative research studies in the current diagnostic program are concerned with the use of cytology as a method for detecting cancer of other sites including the digestive tract and genito-urinary system. Cost of all 11 direct cooperative research studies is estimated at $663,000.

CHEMOTHERAPY RESEARCH

Clinical trials show alkaloid, VLB, promising against choriocarcinoma

In previous studies in the Endocrinology Branch, Vincaleukoblastine (VLB) was found to inhibit human choriocarcinoma, a rare, highly malignant tumor of the uterus arising during or after pregnancy, transplanted into the cheek pouch of hamsters. On the basis of this observation, eight women with the disease were treated with VLB by scientists of the Endocrinology Branch. All of the patients had developed resistance to methotrexate and to several other antitumor agents.

Vincaleukoblastine is an alkaloid originally derived from the periwinkle plant in 1957 by Cutts, Beer, and Noble, of the Collip Research Laboratories, University of Western Ontario, London, Ontario, Canada. The anticancer activity of VLB in mice was also investigated by Dr. Irving S. Johnson of the Eli Lilly Co. The first clinical trials were carried out simultaneously at Indiana University Medical Center, at Ontario Cancer Institute, and at the National Cancer Institute. The drug was provided for research purposes by Eli Lilly Co.

In the present study, reported by Dr. Roy Hertz, the eight women received intravenously one to six 3-day courses of VLB in varying amounts of 9 to 36 milligrams per course. Therapeutic effect was determined by reduction in the size of metastic lesions and in the level of urinary gonadotropin, a hormone produced by the tumor.

Of the eight women treated, one showed complete remission, which at the time the report was prepared had lasted 6 months. In two others the urinary gonadotropin excretion reached normal levels. Two patients showed regression of pulmonary metastases, and three had no response following administration of VLB.

Some of the side effects observed in all patients were suppression of the bone marrow when total VLB dosage reached 30 milligrams, hair loss, and severe mental depression. Inhibition of the deep tendon reflexes occurred in five patients and fever in six. All toxic effects proved reversible following each course of therapy.

Results of other clinical trials reported in the scientific literature suggest that the potentialities of VLB should be explored further for the treatment of acute leukemia and Hodgkin's disease.

Sarcolysin promising against varying types of malignant tumors

Dr. Bernard J. Miller of Jefferson Medical College has reported results of a study showing that favorable effects can be obtained in patients by admininstration of a derivative of nitrogen mustard, commonly known as sarcolysin.

A group of 60 patients with far-advanced malignant tumors were given the drug orally (53 patients) or by the isolation-perfusion technique, usually in a dosage of 2 milligrams per kilogram of body weight. Objective evidence of favorable response was a gradual regression of tumor masses, occurring within 2 to 4 weeks.

Sarcomas of varying types, especially Hodgkin's disease were most susceptible to the drug. Next in order of susceptibility were melanomas and carcinoma of the breast. Occasional cases of carcinoma of the lung, tongue, ovary, and colon responded, although for much shorter periods.

At the time the report was prepared, 25 patients were living, 34 were dead, and 1 was lost to followup. The duration of favorable effect among the patients still alive ranged from 8 weeks to 16 months.

Bone-marrow depression in varying degrees was the major side effect. It was observed rarely when the drug was given orally, and more frequently with the segmental perfusion.

Sarcolysin [(p-di-chloroethyl)-aminophenylalanine] was synthesized in 1953 by Russian scientists Dr. L. F. Larionov and his colleagues, who also demonstrated its tumor-inhibitory effects in experimental animals and patients. Dr. O. Creech, Jr., and his colleagues have used the drug in treating patients by the isolation-perfusion technique and have reported favorable effects in melanomas. The scientific literature contains numerous other reports of pharmacological and antitumor studies of sarcolysin and compounds closely related to it.

Other names for sarcolysin are sarcolysine, merphalan, CB 3007, sarcochlorin, and DL-phenylalanine mustard. It is available for research purposes as Sarcolysin from the National Drug Co., Philadelphia.

New hormonelike drug for breast cancer lacks masculinizing activity

In treating certain patients with advanced breast cancer, male sex hormones have been found capable of inducing temporary regressive changes in metastatic lesions. A clinical test of a new compound, delta-one-testololactone, showed that it produced none of the masculinizing side effects usually observed with the male hormone, testosterone, to which it is chemically related. At the same time, in this study its anticancer activity was similar to that of testosterone.

This finding was reported by Dr. Albert Segaloff, Alton Ochsner Medical Foundation, New Orleans, and his associates of the Tulane University and Louisiana State University Schools of Medicine. The study was supported by a grant from the National Cancer Institute and was a part of the program of the cooperative breast group of the Cancer Chemotherapy National Service Center.

The compound was synthesized in 1953 and studied in animals by scientists of the E .R. Squibb & Sons Division of the Olin Mathieson Chemical Corp., New York City. It is available from Squibb for research only.

Delta-one-testololactone was administered intramuscularly to 23 postmenopausal patients with progressive metastatic disease. None of them had received previous horomonal therapy. Regression of most of the lesions and increase in the size of none, as determined by roentgenograms, caliper measurements, and photographs, constituted evidence of objective response to therapy.

Objective response was observed in seven patients. Response occurred in a larger percentage of patients with local or soft tissue metastases than in those with either osseous or visceral involvement.

Scalp hair root damage correlates with toxic effect of anticancer drug

Scientists of the General Medicine Branch have continued their study of changes in scalp hair roots of patients receiving treatment for cancer. Earlier studies showed damage to hair roots following treatment with radiation and the antifolic agent, methotrexate, and an association between the extent of damage and the dose used in therapy.

In the present study reported by Drs. Robert G. Crounse and Eugene J. Van Scott, microscopic examinations were made of growing hair roots obtained from the scalp of patients receiving a variety of chemotherapeutic agents in the clinical services of the National Cancer Institute. In 57 patients effects of the following drugs were studied: 3′,5′-dichloroamethopterin, triethylene thiophosphoramide (thio-TEPA), 6-mercaptopurine, 5-fluorouracil, colcemid, actinomycin D, nitrogen mustard, cyclophosphamide, and Vincaleukoblastine.

Structural damage to hair roots occurred following the administration of the drugs. The essential effect seemed to be inhibition of hair root growth, which was promptly reversible when the drug was discontinued. A close correlation was found between hair root damage and hematologic signs of drug toxicity.

The findings led the investigators to confirm their earlier conclusion that the hair is a sensitive indicator of the toxic effects of chemotherapeutic agents and to suggest that the relatively simple procedure of examining hair roots can be useful in the clinical management of patients receiving such treatment.

Staff scientist reports method of using viral tumors for drug screening

Dr. W. Ray Bryan, of the Laboratory of Biology, has suggested an approach to employing virus-induced animal tumors in the screening of potential anticancer drugs.

Tumors induced by viruses are desirable for screening potential anticancer agents because they derive entirely from the hosts' own tissues, thereby simulating naturally occurring tumors. Since several established viral tumor systems are now available, biologically comparable tumors can be produced in large numbers. These can be used as a basis for increasing the accuracy of measuring chemotherapeutic effects.

A large store of knowledge has emerged from several years of investigation of the biological properties of such viral tumors as the Rous sarcoma of chickens, the Friend leukemia of mice, the Shope rabbit papilloma, and a leukemia of mice recently described by Moloney. Using such information, Dr. Bryan devised several orientation charts, with which an investigator can plan a test program of chemotherapy screening using viral tumors.

The charts show the frequency of animals developing tumors with increasing dilution of virus dose and the smallest amount of virus that produces 100 percent incidence of tumors. They also show the latent period—the time elapsing between virus inoculation and appearance of tumors.

Dr. Bryan reviewed preliminary results of studies at other laboratories using the Rous sarcoma and Friend leukemia systems to show the sensitivity of these tumors in measuring antitumor activity of test compounds. After virus inoculation, antitumor effect was measured by the extent to which a drug delayed the appearance of grossly detectable tumors. It is of interest that many of the compounds showing significant antitumor effects in both these systems are among those found to be most effective in nonviral tumor test systems and in man.

Chemotherapy program reaches new high level of clinical activity

The Cancer Chemotherapy National Service Center was established in 1955 to accelerate research and speed the introduction of promising agents into clinical trial. It has accomplished both goals. Cancer chemotherapy research now constitutes the largest and most comprehensive single approach to solution of the cancer problem; more drugs are being evaluated in the clinic today than ever before.

The clinical phase of the Service Center's program expanded at an unprecedented rate. A total of 50 new compounds was added to the 109 being evaluated a year ago for anticancer activity. Of the 159 drug now in clinical trial, only 31 were in use prior to the establishment of the chemotherapy program almost 6 years ago. Scientists in more than 150 hospitals throughout the United States and Western Europe are conducting some 200 clinical studies, which to date have involved more than 16,500 patients.

Results of a clinical study sponsored by the Service Center indicated that women who received both radical surgery and chemotherapy for breast cancer were substantially less likely to have recurrent disease than were women treated only by surgery. In the study, 107 women, all of whom were considered good candidates for surgical cure, underwent radical mastectomy. Fifty-seven of the patients also received an anticancer drug, thio-TEPA, administered intravenously on the day of operation and on the first and second postoperative days. The remaining 50 received a placebo. Data collected over a 2-year period indicated that 83 percent of the women who received thio-TEPA have remained free of recurrent disease, while only 54 percent of the other group were still free of cancer. Although the results of this study are preliminary, they constitute the first clear-cut evidence that adjuvant chemotherapy can markedly improve the benefits of surgery.

The animal screen—the first step in determining whether a material has anticancer activity—was broadened to help overcome one of the most formidable problems in chemotherapy research: estimating the clinical effectiveness of a drug on the basis of results of animal studies. In addition to the standard three-tumor mouse screen, two transplantable rat tumors (Walker 256 carinosarcoma and Dunning leukemia) were being employed to assess the activity of some types of drugs, particularly alkylating agents. These two tumor systems are useful in predicting the effectiveness of anticancer agents against human leukemias and lymphomas, such as Hodgkin's disease. Tissue culture was added as a screening tool for the study of materials submitted in quantities insufficient for animal testing. Compounds showing activity in tissue culture can be synthesized in larger amounts for study in mice.

Tumors in hamsters and guinea pigs may be employed for screening purposes if current investigations prove them useful. Use of these tumor systems would require substantially increased production of the animals, since chemotherapy screening would use the entire present annual production.

Exchanges of technical information are helping accelerate chemotherapy research. To expedite communication in the field, the Service Center began publication of Cancer Chemotherapy Abstracts, a monthly compilation of abstracts of reports appearing in journals throughout the world. A companion publication, now 2 years old, is Cancer Chemotherapy Reports, which desseminates current information on the status of the program.

The major part of the Service Center's program is carried out under contracts with pharmaceutical firms, research institutions, colleges, and universities. Current obligations for support of active contracts, plus funds needed to activate newly approved contracts, amount to $21,380,000.

OTHER THERAPY

Further studies needed to determine usefulness of radioactive sulfur

Results of clinical studies of the use of radioactive sulfur (S^{35}) against advanced chondrosarcoma, a cartilaginous tumor, were reported by Dr. J. Robert Andrews and his associates of the Radiation and Endocrinology Branches and the Laboratory of Pathology, and by Dr. Raymond G. Gottschalk of the Veterans' Administration Center, Martinsburg, W. Va. Previous studies had shown that S^{35} arrested cartilage growth in experimental animals, and that tracer amounts of the isotope were taken up by human chondrosarcoma.

Dr. Andrews and his associates administered 1 curie of S^{35} intravenously in three doses to a 42-year-old male patient. Radioactivity assays showed significantly higher concentrations of the isotope in tumor tissue than in normal rib cartilage or in skin. Autoradiographs demonstrated uptake of S^{35} by viable tumor tissue, but not by necrotic tumor cells.

Subcutaneous nodules of the tumor stopped growing for 5 months following injection of the S^{35}. The only side effect was temporary, but severe, hematopoiesis. Dr. Andrews concluded that the dose administered may have produced a temporary halt in growth of the chondrosarcoma.

In the study conducted by Dr. Gottschalk and his associates, three patients received doses ranging from 559 to 926 millicuries of S^{35} in the form of sodium sulfate in three to six intravenous injections. In two of the patients, the rate of growth of the chondrosarcomas appeared reduced for several months. Otherwise, the results were similar to those reported by Dr. Andrews.

These findings indicate a need for studies of additional cases of chondrosarcoma, which may have different degrees of radiosensitivity or isotope uptake, to determine whether S^{35} can regularly produce significant palliation in some cases.

New technique reveals status of urine flow through ileal bladder

Scientists of the Surgery Branch have previously reported the successful clinical use of the ileal bladder as a means of urinary diversion in patients whose normal urinary bladder function stops as a result of disease or surgery. Use of the ileal bladder, however, creates an abornmal anatomical arrangement and makes difficult the evaluation of the upper urinary tract.

Dr. James R. Jude has now reported a method in which a series of radiographs is made of the ileal bladder following introduction of a radiopaque dye. Findings in a study of 15 patients show that failure of the ureters to fill with the dye does not necessarily imply that an anatomical obstruction is present. A fortuitous valvelike action may be present, preventing regurgitation of the dye up one or both ureters. The investigators conclude that when the cause of postoperative hydronephrosis needs to be determined, these retrograde urinary ileograms together with the usual excretory urograms provide valuable information as to the status of the ileal bladder urinary diversion.

SURVIVAL OF CANCER PATIENTS

Connecticut figures show survival rate of uterine cancer patients improving

Women with cancer of the uterus have a better chance of surviving today than they had 25 years ago, and the improvement may be associated with increased use of surgery in treating this disease. This is a recent conclusion based on analysis of data on life expectancy of cancer patients in Connecticut between 1935 and 1954. Earlier diagnosis resulting from physicians' use of cytologic, or cell examination, test may also have contributed to the improvement in survival of uterine cancer patients.

Survival in ovarian cancer has not improved significantly in the last 25 years. In both ovarian and uterine cancer, the outlook for younger women is better than that for older women.

The analysis of survival experience was made by scientists of the Biometry Branch, in collaboration with investigators of the Connecticut State Department of Health. The data that were comprehensively analyzed consisted of the medical records of all cancer patients (more than 75,000) in Connecticut between 1935 and 1954. The figures on survival were compared with those reported from a number of other treatment centers throughout the country. Because the findings in Connecticut were virtually identical with those reported elsewhere, they are considered to be representative of the entire United States.

Dr. Sidney J. Cutler reported that the results confirmed those obtained in the preliminary analysis of crude data reported in a monograph, "Cancer in Connecticut—1935–51," which was prepared in 1955 by the Connecticut State Department of Health under a grant from the National Cancer Institute. That study showed that the ratio of cancer patients surviving 5 years after diagnosis had risen from 1 in 4 at the beginning of the reporting period to 1 in 3 at the end of the period. It also showed that among patients treated surgically for localized uterine cancer, the 5-year survival rate was nearly 90 percent.

Five-year survival rates better for women cancer patients than for men

Significant findings in survival rates for lung cancer patients were reported by the End Results Evaluation Section of the Cancer Chemotherapy National Service Center to the Fourth National Cancer Conference in Minneapolis. Data for microscopically confirmed, localized lung cancer diagnosed during or after 1965 and treated by surgery, showed that 5-year survival rates for 116 women and 650 men were 62 percent and 30 percent, respectively. The sex difference was approximately the same for both adenocarcinoma and squamous cell carcinoma of the lung.

Additional data, reported in Public Health Service publication No. 789, "Survival Experience of Patients with Malignant Neoplasms," showed that 5-year survival rates were significantly higher for women than those for men with cancer of the thyroid gland, tongue, and salivary gland, for skin melanomas, and for Hodgkin's disease. Furthermore, significant increases since 1951 in 5-year survival were reported for five sites: large intestine, rectum, and thyroid, for both sexes, and for uterine cervix and corpus.

These findings are highlights of a study of the survival experience of 212,638 cancer patients, based on data submitted by 99 hospitals participating in the cancer end results evaluation program sponsored by the National Cancer Institute. The goal of the program is to facilitate meaningful evaluation of end results in cancer, and particularly to compare the results of surgery and radiation with those of chemotherapy.

Data are compiled in accordance with a uniform code and submitted annually to the End Results Evaluation Section by 10 individual hospitals and the cancer registries of California, Connecticut, Massachusetts, and the Veterans' Administration. Each year, followup data are submitted, and about 50,000 new cases are added. Thus, information is now available on about 300,000 patients. Detailed analyses of some of the data will be published in 1961 by the National Cancer Institute.

This program will form the basis of the U.S. contribution to an international comparison of end results at the Eighth International Cancer Conference to be held in Moscow in 1962. The international program is a collaborative effort by scientists of the National Cancer Institute and some of their colleagues from Great Britain, France, Denmark, Finland, Norway, and Russia.

Bone changes resulting from leukemia described

The bony changes resulting from acute leukemia, with direct correlation between X-ray findings and histological abnormalities, have been described in a collaborative study by National Cancer Institute and Clinical Center investigators.

Drs. Theodore F. Hilbish and his associates of the Clinical Center's Diagnostic X-Ray Department; and Louis B. Thomas, Pathologic Anatomy Branch, and Claude E. Forkner, Jr., General Medicine Branch, both of the National Cancer Institute, reported the results, which formed the basis of an exhibit that was shown at the 107th meeting of the American Medical Association.

The findings showed multiple areas of bone destruction, radiolucent bands, particularly in children, some new bone formation, and heavy leukemic infiltration. Growth lines were often demonstrated in patients experiencing periods of remission following antileukemic therapy.

Staff scientists report study of brain hemorrhage in patients with leukemia

Dr. Emil J. Freireich, General Medicine Branch, and his colleagues of the National Cancer Institute have reported detailed studies of fatal intracranial hemorrhage in patients with acute leukemia whose leukocyte counts rose to more than 300,000 per cubic millimeter. An earlier paper reported the observation of a distinctive hemorrhagic lesion largely confined to the white matter of the brain in such patients. In leukemic patients who died of intracranial hemorrhage but whose blood counts were lower than 300,000, the hemorrhage was primarily subdural or subarachnoid, as seen in nonleukemic patients with thrombocytopenia.

Intracerebral nodules of leukemic cells and stasis of leukemic cells (leukostasis) in small intracerebral vessels were found only in patients with leukocyte counts of more than 300,000. Neither leukostasis nor leukemic nodules were found in patients with leukocyte counts below 100,000 per cubic millimeters. The data suggest that local intravascular growth of leukemic cells results in destruction of the vessel wall and formation of a leukemic nodule. Finally, hemorrhage occurs about the nodule and coalescence of many such lesion results in the large hemorrhage seen grossly. This intracerebral leukemic lesion is the major factor responsible for fatal intracranial hemorrhage in patients with high leukocyte counts.

Spinal fluid examination shows onset of syndrome of meningeal leukemia

Investigators of the General Medicine and Pathologic Anatomy Branches have continued their detailed studies of the natural history of acute leukemia, particularly neurological complications. Dr. Edward W. Moore has reported results of a postmortem study of the central nervous system of 117 patients admitted to the Clinical Center.

Twenty-three (19 percent) of these patients showed the clinical syndrome of meningeal leukemia. Any patient with acute leukemia may develop the meningeal syndrome, but it is most frequently noted among boys with acute lymphocytic leukemia.

The pathological findings showed that this syndrome is related to the leukemic infiltration of the arachnoid, particularly along the brain stem, and to internal hydrocephalus. The leukemic infiltration within the arachnoid probably interferes with the flow of cerebrospinal fluid (CSF) and results in increased intracranial pressure.

The degree of leukemic infiltration of the arachnoid is reflected in the CSF. Dr. Moore suggests that examination of the CSF should allow for early recognition and treatment, with the possible prevention of hydrocephalus and other irreversible neurological lesions.

Comprehensive study of meningeal leukemia suggests treatment method

The work was extended by the same group of scientists to a comprehensive study of meningeal leukemia, which was observed in 25 of 150 acute leukemia patients admitted consecutively to the Clinical Center during a 5-year period ending April 1, 1958.

Dr. Richard K. Shaw reported that meningeal involvement is primarily a complication of acute lymphocytic leukemia in children. The syndrome may occur at any stage of the disease: as an initial manifestation, during hematologic remission, or during an active leukemic phase. Its appearance is indicative of relapse.

A diagnosis of meningeal leukemia is confirmed by examination of the cerebrospinal fluid showing increased pressure, presence of leukemic cells, and absence of infection. The characteristic radiologic finding is spreading of the cranial sutures in children.

A literature review included in the present report shows that meningeal leukemia has become more common since the advent of chemotherapy. Only 31 patients were reported between 1878 and 1948, in contrast to 69 between 1949 and 1959. The increase is partly related to the ability of antimetabolites to prolong the lives of acute leukemia patients, particularly children. Of 21 children in the Clinical Center group, 113 developed the meningeal syndrome more than 4 months after onset of leukemia. It appears that the failure of antimetabolites to cross the blood-brain barrier may play a role in the development of the meningeal syndrome.

The investigators recommend treating meningeal leukemia first with adrenal steroids administered systemically; then, if additional therapy is indicated, with whole brain irradiation or methotrexate injected into the spinal fluid.

Negative trial of drug provides data on course of human acute leukemia

The importance of scientifically designed studies in chemotherapy was highlighted by a collaborative study reported by National Cancer Institute investigators and their colleagues of the Acute Leukemia Cooperative Group B, sponsored by the Cancer Chemotherapy National Service Center.

During a previous study of the toxicity of a new anticancer drug, 6-azauracil, Institute scientists observed objective hematologic improvement in five leukemia patients whose disease on longer responded to conventional chemotherapy (e.g., folic acid antagonists, adrenocortical steroids, or purine analogs). A comparative study was, therefore, designed to evaluate the therapeutic efficacy of the drug in patients with advanced refractory acute leukemia.

Dr. Emil J. Freireich, General Medicine Branch, reported that eight children and seven adults received 6-azauracil while seven children and six adults received placebo. Although partial remissions were observed for varying periods in four patients in each group, the difference between the two groups in median survival time was not significant.

These findings provided an unusual opportunity to obtain information about the natural history of advanced refractory acute leukemia. A significant proportion (30 percent) of the patients showed objective hematologic improvement even in the absence of effective specific therapy. The patients had a median survival of 2 months from the start of the study, and children and adults showed similar survival patterns.

The toxicity of 6-azauracil limited the clinical dose to less than 10 percent of that (on a weight basis) producing antitumor effects but not toxicity in animals. These findings provide a rationale for further studies of a derivative of 6-azauracil, azauridine, which preliminary clinical studies show is better tolerated than the parent compound.

The compound, 6-azauracil, an antimetabolite, was supplied by E. R. Squibb & Sons, New Brunswick, N.J. It was synthesized in 1955 and shown to have antitumor activity in animals by Dr. Arnold D. Welch and his associates of the Yale University School of Medicine. Preliminary clinical studies reported in 1957 by scientists of the National Cancer Institute and the District of Columbia General Hospital suggested that the compound had some therapeutic activity in acute leukemia.

Study of how 6–MP acts increases understanding of drug-resistant tumors

Studies of the mechanism of action of the antitumor agent, 6–mercaptopurine (6–MP), are important to an understanding of resistance to the drug and to development of more effective derivatives. Results of one such study, summarizing data on the effects of 6–MP upon nucleic acid metabolism of mouse leukemia L1210 cells in vitro, have been reported by Dr. Jack D. Davidson of the General Medicine Branch.

Drug-sensitive and drug-resistant leukemic cells were compared with respect to utilization of radioisotopic precursors for the formation of nucleic acid purines. Both lines showed similar rates of nucleic acid synthesis, but the details of the metabolism were different. The sensitive line showed much greater utilization of labeled hypoxanthine (purine precursor); utilization for adenine formation was greater than for guanine formation. Resistant cells utilized labeled glycine (amino acid precursor) to a greater extent than the sensitive ones, and the utilization for guanine formation was greater than for adenine.

6–MP, which is similar to hypoxanthine except for the substitution of a mercapto (SH) group for a hydroxyl (OH) group, inhibited the incorporation of hypoxanthine and glycine into the adenine nucleotides (moieties of nucleic acid) in the sensitive cells, but had no effect on the guanine nucleotides. These findings support the hypothesis that 6–MP is metabolized to its nucleotide, and this produces a metabolic block in the conversion of inosinic acid (hypoxanthine nucleotide) to adenylic acid (adenine nucleotide). The common pathway for these two precursors lies between inosinic acid and adenylic acid.

In the resistant cells, 6–MP inhibited profoundly the incorporation of hypoxanthine into both the adenine and guanine moieties; utilization of glycine was unaffected. These results suggest that the 6–MP block in the resistant cells is located on the pathway from free hypoxanthine to inosinic acid. This pathway is of limited capacity in the resistant cells and is incapable of producing sufficient 6–MP nucleotide to inhibit the conversion of inosinic acid to adenylic acid. Resistance is, therefore, correlated with the cell's loss of the capacity to convert free 6–MP to its nucleotide derivative, which appears to be the form responsible for antitumor activity.

Drugs used to treat mice with systemic leukemia may also confer immunity

Dr. Abraham Goldin of the Laboratory of Chemical Pharmacology has reported further results in the continuing studies of the effectiveness of dihalogenated derivatives of methotrexate in prolonging the life of mice with transplanted leukemia L1210.

The current study of immunity in mice surviving the systemic disease confirms preliminary findings that many of the long-term survivors are markedly immune to reinoculation of leukemic cells, the new inoculum showing no, or very slow, growth. Other data suggest that the leukemia must be sufficiently far advanced, possibly systemic, for eradication of the disease by treatment with the drugs to be accompanied by the development of immunity.

Dr. Goldin concludes that the drugs act, at least in part, by influencing the host-tumor relationship so that the mice become immune. Thus, the importance of understanding the interrelationships of the host tumor, and drug in the chemotherapy of cancer is again emphasized.

Scientists continue study of host-tumor-drug factors in L1210 mouse leukemia

Additional results of the study of the interrelationships of host-tumor-drug factors in the L1210 mouse leukemia were reported by Dr. Goldin. The finding that mice surviving systemic leukemia L1210 following treatment with drugs showed immunity to reinoculation of drug-sensitive and drug-resistant sublines of the leukemia suggested another line of investigation. This was the possibility of utilizing the immune response to enhance the effectiveness of chemotherapy of mice bearing variant forms of the disease resistant to specific drugs or classes of drugs.

Mice were inoculated on day 0 with a subline, L1210Z, which is sensitive to therapy with antifolic drugs, and on day 7 with a subline, M46R, which is resistant to antifolic drugs. Treatment with 3′, 5′-dichloroamethopterin (DCM), started on day 7, when the sensitive disease had become systemic, produced a median survival time of approximately 40 days from the day of inoculation of the resistant subline.

On the other hand, the survival time of DCM-treated mice bearing only the resistant subline did not exceed 20 days, even if treatment was started on the day of implantation. Furthermore, if the mice were inoculated with both lines and treatment was started on the same day, they survived no longer than treated mice bearing only the resistant subline.

The findings showed that it was possible to prolong the survival of mice bearing an antifolic-resistant variant of leukemia L1210 and receiving treatment with DCM by prior inoculation with a drug-sensitive subline. The presence of systemic sensitive leukemia L1210 appeared to elicit in the hosts an immune response, which contributed to the therapeutic effect of DCM against the resistant variant. Further study of the relationship of drugs to immunological inhibition and enhancement is continuing to learn if it offers a basis for improved cancer therapy.

STUDIES AT THE CELLULAR LEVEL

Cancer cells in blood seen more frequently in inoperable patients

Dr. John F. Potter and his colleagues in the Surgery Branch, working with scientists in the Pathologic Anatomy Branch, have reported the latest results of a continuing study of the significance of cancer cells in blood.

Blood from 376 cancer patients provided the source material for the study. Specimens of peripheral blood or venous blood draining the tumor site at the time of operation were examined by a quantitative technique described by Institute scientists about 2 years ago for processing human whole blood so that it can be studied microscopically for the presence of malignant cells.

Malignant cells were found in the peripheral blood in 28 percent of 285 patients and in local blood (at the tumor site) of 43 percent of 91 patients. There was a significantly greater frequency of cancer cells in both peripheral and local blood of patients with nonresectable cancers than in those in the resectable group.

Scientists continue study of effects of radiation on human cancer cells

Dr. Robert E. Bases, of the Radiation Branch, has reported that the antibiotic, actinomycin D, enhanced the killing effects of X-rays on single HeLa cells (human cancer cells grown in tissue culture) exposed to the drug just before or after irradiation and during clone formation. This laboratory investigation was prompted by an interest on the part of scientists in modification of the response of mammalian cells to ionizing radiation and by the observation that actinomycin D apparently produces an enhanced response to radiation therapy in cancer patients.

In the present study, actinomycin D was not unique in producing this response, as cells in culture medium containing a large percentage of heavy water (D_2O) were also more sensitive to radiation. In fact, prolonged exposure to D_2O (14 hours) enhanced the radiation sensitivity of the cells even after D_2O was removed.

Majority of cells repair X-ray damage before they divide

Continuing his studies of the effect of radiation at the cellular level, Dr. Mortimer M. Elkind, of the Radiation Branch, has reported on studies of X-ray damage and recovery in mammalian cells carried in tissue culture.

Other studies reported in the scientific literature have suggested that X-ray damage may be cumulative. It follows, therefore, that surviving cells having accumulated a sublethal amount of damage might be more sensitive to subsequent exposure to X-ray than the parental population.

To investigate the question of the presence of heritable damage, the effect of X-ray on two lines of Chinese hamster cells propagated in tissue culture was studied. The vast majority of surviving cells did not transmit sublethal damage to their progeny, but completely repaired their accumulated damage before their first division after irradiation. Also, surviving cells could undergo repeated cycles of damage and repair with no apparent weakening of the repair process.

Nucleic acid different in normal and leukemic human white blood cells

Results of a study of nucleic acid (DNA) from human normal and leukemic tissues have been reported by Dr. G. di Mayorca at the Sloan-Kettering Institute for Cancer Research. DNA is of particular interest at the present time because of the concept that this important component of cells is the focal point of the origin of cancer and the target of chemotherapy.

Chemical analysis showed that DNA obtained from normal spleen and leukocytes was similar to that from leukemic leukocytes. However, analysis by anion-exchange chromatography showed that the DNA of normal spleen is somewhat different structurally from that of normal leukocytes. Furthermore, the DNA of normal leukocytes is markedly different from that of leukemic leukocytes. In turn, the DNA of leukocytes from patients with chronic granulocytic leukemia differs from that from patients with chronic lymphatic leukemia.

Previous reports in the scientific literature have shown that the DNA of human leukocytes is structurally heterogeneous. The present study extends these findings to the DNA of the leukocytes of untreated leukemia patients and the DNA of normal human spleen.

Human and other sera lethal to mouse tumor cells studied in vitro

Dr. Maurice Landy, Laboratory of Chemical Pharmacology, reported results of a comprehensive study showing that normal serum from human and many other species exerts a lethal effect on mouse tumor cells in vitro.

Human serum interacted in the test tube for 1 hour at 37° C. with sarcoma 37 ascites tumor cells in the proportion of 1 million cells to 1 ml. of serum affected the cells so that they failed to proliferate in mice; control cells gave rise to progressive growth of tumor within 8 to 12 days. Other evidence of damage by normal human serum to S–37 cells was manifested by their loss of metabolic activity, inability to exclude dyes, and changes in their structure. Of several serum components which participate in the damaging effect on tumor cells, "normal" antibody is the specific one.

These damaging effects on S–37 tumor cells were produced by serum of 11 of 17 animal species examined.

Cells of about a dozen mouse and rate tumors were capable of absorbing the "normal" antibody from human serum. The antibody was absorbed also by lymphoid tissues of mice—spleen, lymph nodes, thymus, and bone marrow—suggesting that these tumors and lymphoid tissue posses a common antigen.

It was concluded that there is thus "widely distributed among animals a type of 'natural' antibody, which * * * may serve as a barrier against invasion by cells of foreign species."

Technique is described for determining origin of cultured cell lines

The planned use of cultures of living cells in studies of the viral etiology of human cancer has highlighted the need for characterizing established cell lines. Currently almost 100 different kinds of cells are under cultivation in laboratories throughout the country. Under the auspices of the National Cancer Institute Viruses and Cancer Panel, a Cell Culture Collection Coordinating Committee was recently established under the chairmanship of Dr. Jerome T. Syverton, University of Minnesota, for the purpose of characterizing, standardizing, and preserving mammalian cell lines.

Dr. Vittorio Defendi, of the Wistar Institute of Anatomy and Biology, has reported that immunological and karyological (chromosome morphology and constitution) characteristics gave sufficient information to identify 11 established cell lines in vitro. No criterion alone was sufficient, but together the criteria corroborated each other.

In the study now reported, three characteristics were found to be highly indicative of the originating species of a given cell line. These were: (1) Sensitivity to nucleoprotein antiserums, indicating antigen-antibody combination. Whether or not cells of the line under test were destroyed by the antiserums showed that the cell line was of human or murine origin. (2) Sensitivity to skin grafts from C3H mice, indicating the presence of murine transplantation antigens. Adult mice of a selected inbred strain were inoculated intraperitoneally with cells of the test line. Some days later the mice were given skin grafts from a donor of a different inbred strain. Curtailed survival of the grafts indicated the sharing of at least one important transplantation antigen between the test cells and the strain providing the skin grafts, and thus showed that the line under test was of murine origin. (3) Chromosome studies.

Of the 11 cell lines studied, four—three of stated human origin and one of stated rabbit origin—were found to be of mouse origin, probably consisting of L cells. Dr. Defendi suggested that these four cell lines represent contaminations from L cells, which appear to have exceptional ability to survive.

Four similar human cell lines differentiated by responses to chemicals

Another study conducted by scientists of the Laboratory of Chemical Pharmacology was concerned with the differentiation of morphologically similar cell lines. Such cell lines are commonly characterized by nutritional requirements, chromosome counts and anomalies, sex-chromosome markers, morphologic variations, immunologic response, and virus susceptibility.

Henry C. Orr and Dr. Morris Belkin have reported the possibility of characterizing four morphologically indistinguishable cell lines by their response to certain chemicals. The strains are: HeLa, a line of malignant cells derived from a patient with uterine cancer, and three cell lines, designated as D227, D189, and D164, which resulted from spontaneous in vitro transformations of normal human fibroblasts into cells histologically similar to malignant cells.

Strain D227 was the only line to respond to Suramin sodium. After 1 to 2 days' exposure to this compound, D227 exhibited a number of changes, including fragmentation and beading of the cell membrane.

Pronounced vacuoles appeared in the cytoplasm of cells of strain D189 after 3 days' exposure to 0.01 mg. of hydrocortisone per ml. of nutrient medium. Exposure to a tenfold dose of hydrocortisone for 10 days produced sporadic vacuolization in D164 cells and cellular enlargement and nuclear aberration in HeLa cells.

These findings demonstrate that the strains are free from cross-contamination and suggest that the D derivatives represent completely different biological variants.

TUMORS IN LABORATORY ANIMALS

Carcinogens found most active in newborn mice

Confirmation of the extraordinary susceptibility of baby mice to carcinogenic stimuli was afforded by work by Dr. Roger W. O'Gara, Laboratory of Pathology, and Dr. Margaret G. Kelly, General Medicine Branch. They reported that microgram quantities of carcinogenic hydrocarbons introduced subcutaneously into newborn randomly bred Swiss mice produced pulmonary tumors in all of them within 16 weeks. Similar results were obtained in two inbred strains of mice with low spontaneous incidence of pulmonary tumors. The number of pulmonary tumors obtained from exposure to the carcinogen on the first day of life was substantially greater than that from the same dose injected at 1, 3, or 6 weeks of age. In addition to the pulmonary tumors, some mice developed subcutaneous fibrosarcomas. Tumors of the sebaceous glands, adrenal cortex, and liver appeared, as well as leukemias and lymphosarcomas.

Small amounts of X-ray prevent growth of mouse tumor cells as metastases

In a search for more effective means of dealing with the dissemination of viable cancer cells during surgery, scientists of the Surgery Branch conducted a laboratory study of the efficacy of small amounts of radiation in decreasing the production of metastases.

Dr. Robert C. Hoye reported that amounts of radiation ranging from 170 to 2,000 r. produced an apparent change in the cells of four transplanted mouse tumors without significantly altering the growth of the tumors themselves. The cellular change prevented the growth of the majority of cells as lung metastases, when the cells were artificially disseminated from the host tumor 24 hours following radiation.

The mechanism responsible for this change in growth potential of disseminated cells is not yet known.

Fibrinolysin inhibits pulmonary metastases in tumor-bearing rats

Dr. Carlo E. Grossi at the Sloan-Kettering Institute for Cancer Research reported that human fibrinolysin effectively inhibited the development of pulmonary metastases in a large percentage of rats bearing the Walker 256 carcinosarcoma.

Rats were injected first with fibrinolysin solution and then within a few minutes with suspensions containing large numbers of tumor cells. The animals were sacrificed when they seemed about to die or at the end of 9 weeks. Gross autopsy was performed in all animals.

Only 25 percent of 113 treated animals were found to have metastatic deposits in the lungs. In contrast, 81.5 percent of 103 control animals developed one or more pulmonary metastases. The liver, spleen, and other organs appeared normal in both groups.

Dr. Grossi suggested that the existence of fibrinolytic activity at the time of inoculation of tumor cells prevented the tumor cells from lodging in the lungs. He suggested further that clumping of cells may be necessary for lodging of cells and that fibrin formation may maintain them until metastatic growth can take place.

Institute study shows growth-stimulating factor in tumor is sodium ion

Previous studies by scientists of the Laboratory of Physiology have shown that tumor-bearing rats fed a diet containing lyophilized tumor tissue consume more food and water, gain more weight, and produce larger tumors than do rats receiving casein.

Dr. Julius White reported that the growth stimulatory properties of Walker carcinosarcoma 256 tissue were shown also by the water-soluble fraction prepared from it, and that the factor principally responsible for the activity was sodium ion. Addition of sodium chloride to the water-insoluble fraction of Walker 256 tumor tissue and to the casein diet resulted in markedly increased water intake, food intake, and weight gain.

RELATED FUNDAMENTAL STUDIES

Antibody activity found in fractions 1 and 5 of human gamma globulin

Dr. John L. Fahey, General Medicine Branch, has reported further results in his study of the nature of gamma globulins from human blood. In an earlier report, he described their isolation from the rest of the normal blood serum proteins and their fractionation by the technique of anion-exchange cullulose chromatography. Ninety to 95 percent of the gamma globulins comprised a heterogeneous group of protein molecules of about the same molecular size; these were separated into four fractions, which differed in electrical charge and carbohydrate content. A fifth fraction contained 5 to 10 percent of the gamma globulins and although comprised largely of protein macromolecules (giant size molecules) also included a small amount of the smaller molecules.

In the present study, the distribution of normal and abnormal physiologic activities among the five gamma globulin fractions was investigated. Antibodies to mumps virus, Histoplasma capsulatum, thyroglobulin, and typhoid H antigen were found in fraction 1. Antibiodies to the rheumatoid arthritis factor and typhoid 0 antigen were found in fraction 5. Several activities were found in fractions 1 and 5—anti-A and anti-B isohemagglutinins, the Rh antibodies, and the anti-liver-nucleoprotein extract activity, when present in the serum of patients with lupus erythematosus. The finding of the same activity in two fractions indicated that the antibody activity was associated with distinctly different gamma globulin molecules.

Dr. Fahey reported that fractions 2, 3, and 4, comprising about 20 percent of the total gamma globulins, could not be demonstrated to contain the major component of any physiologic activity.

Growth pattern studied in rats after removal of pituitary gland

Dr. Roy Hertz, Chief of the Endocrinology Branch, has reported detailed studies on the growth pattern in young rats which were hypophysectomized (pituitary gland removed). Then multiple pituitary grafts were implanted underneath the kidney capsule in the rats from which the pituitary was removed. The grafts supported substantial somatic growth—about two-thirds the normal rate—but failed to maintain normal thyroid, adrenal, and gonadal function.

These results contribute to clarification of the relationship between hypothalamus and pituitary, and show that in the rat, production and secretion of the growth hormone are not completely dependent upon an intact hypothalamic-pituitary system. Dr. Hertz suggests that such pituitary grafts, which are known to increase the incidence of breast cancer in mice, may exert their tumor-enhancing effect at least in part by producing growth hormone. Moreover, the data indicate that the demonstrated beneficial effects of the removal of the pituitary stalk in breast cancer patients may not be mediated through suppression of growth hormone.

Age of person affects amount of acid-soluble collagen in human skin

Dr. William G. Banfield, Laboratory of Pathology, has reported that the amount of acetic acid-soluble collagen present in human abdominal skin varies in an orderly fashion throughout life.

Collagen is the main supportive protein of skin, connective tissue, and bone. The changes in collagen in relation to age and pathologic conditions are being investigated in order to arrive at an understanding of its formation and metabolism. An earlier study reported by Dr. Banfield showed that there is a sharp drop in the concentration of soluble collagen in human skin at 1 year of age.

The results of the present study show that until age 20 soluble collagen gradually decreases, from age 20 to 40 it decreases more sharply, and then rises again. At 60 to 80 years of age, 80 percent of individuals whose skin was tested showed soluble collagen. After age 80, soluble collagen declines slightly.

The author speculates that part of the change in solubility of collagen may be the result of a changing hormone pattern, reflected in the collagen metabolism. The actual change that takes place in the collagenous composition resulting in variations in solubility is not yet clear.

New way to prepare slides for electron microscopy reported

Dr. Albert J. Dalton, Laboratory of Biology, has reported a simplified method of staining thin sections of biological material with lead hydroxide for electron microscope studies.

Essentially the technique consists of staining specimens with lead acetate in solution and then exposing them briefly to ammonium hydroxide vapors. Dr. Dalton found that electron micrographs taken of specimens prepared in this way were at least equal in resolution and contrast to those obtained by the more involved procedure of staining with a solution of lead hydroxide, described about 2 years ago in the scientific literature.

EXCHANGES OF RESEARCH INFORMATION

Cancer experts report at quadrennial meeting of national conference

The Fourth National Cancer Conference was held in September at the University of Minnesota, sponsored jointly by the National Cancer Institute and the American Cancer Society. About 1,500 scientists and physicians attending the quadrennial meeting heard reports by the nation's leading cancer authorities and experts from Great Britain, Denmark, Russia, and other foreign countries.

Over 90 scientific papers were presented at general sessions which dealt with causation, development and spread, and treatment, and in symposia on the state of knowledge of cancer of specific sites and the problem of cancer control.

A feature of the conference was a special evening program, "Cancer in the World Around Us," to which the public was invited. The speakers discussed environmental factors associated with the occurrence of cancer, such as air pollution, industrial hazards, food additives, radiation, and smoking.

Highlights of the scientific reports included statistical data on the association of smoking, alcohol consumption, childbearing, and dietary habits with the occurrence of various kinds of cancer; improved prognosis of Hodgkin's disease, with statistics obtained in a series of 285 patients showing that 20 percent survived at least 25 years and more than a third survived at least 5 years; increased survival rates in the past 25 years for women with six relatively common forms of cancer of the reproductive and digestive systems, with an exception noted for breast cancer in which no significant improvement in survival has been noted; a 50 percent cure rate for patients with localized lung cancer treated by surgery; evidence that women who undergo surgery for localized lung cancer are twice as likely as men to live at least 5 years after the disease is diagnosed.

Of the 30 scientific exhibits at the conference, the National Cancer Institute cosponsored 2 with the American Cancer Society: a visual presentation of the conference theme "Changing Concepts Concerning Cancer" and a display of books, journals, and publications on cancer. The Institute contributed exhibits on "Virus-Cancer Research" and "International Aspects of Cancer."

The proceedings of the conference are to be published in book form by J. B. Lippincott Co.

Five Soviet scientists visit Cancer Institute

A Soviet delegation of five scientists engaged in cancer research made a 3-day visit to the National Cancer Institute in September under an agreement between the United States and Russia for cooperation in exchanges in the scientific and cultural fields in 1960 and 1961.

The delegation, headed by Dr. Nicolai Blokhin, president of the Academy of Medical Sciences, Moscow, had previously visited the Memorial Sloan-Kettering Cancer Center, New York City. The visitors talked with National Cancer Institute scientists, observed research projects, and presented some of their recent findings in tumor virus and experimental chemotherapy research at a meeting sponsored by the Institute.

NCI monographs present conference proceedings, series of related papers

The Journal of the National Cancer Institute has published to date four National Cancer Institute monographs. The monographs present the proceedings of conferences and symposia, and series of papers dealing with cancer and closely related research fields. They are for sale by the Superintendent of Documents, Government Printing Office, Washington, D.C.

The titles in the series are: No. 1, "Estrogen-Induced Tumors of the Kidney in the Syrian Hamster" (December 1959); No. 2, "Symposium on Normal and Abnormal Differentiation and Development" (March 1960); No. 3, "Conference on Experimental Clinical Cancer Chemotherapy" (August 1960); and No. 4, "Symposia—Tumor Viruses" (September 1960).

The Journal of the National Cancer Institute is distributed in 75 countries, including the U.S.S.R. Approximately 18 percent of the papers describe research findings of investigators in foreign countries. The Journal, established in 1940, was published bimonthly for 16 years, and since July 1956 has appeared monthly.

STAFF AND PROGRAM CHANGES

Dr. Kenneth M. Endicott heads realigned staff

Dr. Kenneth M. Endicott, formerly National Institutes of Health Associate Director for Training, became Director of the National Cancer Institute July 1. He succeeded Dr. John R. Heller who, after nearly 30 years in the Public Health Service, became president of the Memorial Sloan-Kettering Cancer Center in New York City. Dr. Heller served as Director of the Institute for 12 years.

A realinement of administrative responsibility for grant support of research and training, and for field studies, became effective in September with the appointment of two Associate Directors. Dr. Ralph G. Meader, Chief of the Research Grants Branch since 1948, was designated Associate Director for Grants and Training. Dr. Michael B. Shimkin, Chief of the Biometry Branch since 1954, was named Associate Director for Field Studies.

Dr. Stuart M. Sessoms, who has supervised the Institute's worldwide drug development program since November 1958, was also given the title of Associate Director and continues to head the Cancer Chemotherapy National Service Center.

Full responsibility for administration of intramural clinical research was given to Dr. Charles G. Zubrod. Dr. Carl G. Baker, Assistant Director, was assigned responsibility for intramural nonclinical research. Dr. G. Burroughs Mider, now Director, Laboratories and Clinics, National Institutes of Health, formerly administered both of these areas of intramural cancer research. Dr. Eli M. Nadel, formerly assistant to the Associate Director for Intramural Research, National Institutes of Health, was appointed an Assistant Director of the National Cancer Institute.

Institute now awards clinical traineeships to educational centers

Under a new procedure for administration of its clinical traineeship program, the National Cancer Institute awarded 143 grants, totaling $1,059,401, to teaching hospitals and medical research centers throughout the country for advanced training of physicians in the diagnosis and treatment of cancer. The grants were awarded on recommendation of the National Advisory Cancer Council and became effective in July.

The grantee institutions selected the individuals to be trained and set their stipends according to the applicable salary scale. Stipends formerly were awarded directly to the individuals after they had been accepted by their chosen places of training.

More than 200 physicians in about 80 institutions are currently being trained under the program, which was established in 1937. Their fields of study include pathology, radiology, surgery, and internal medicine. Trainees are graduate physicians under 40 years of age who have had at least 2 years' prior training.

Funds to build research facilities are available on nonmatching basis

A total of $5 million from the National Cancer Institute's 1961 appropriation has been allocated for grants to research institutions to pay the cost of construction of facilities for research on cancer. The program is authorized for 1 year only. Grantees are not required to match the awards, but their ability to supplement them is considered in reviewing applications.

Eligible institutions are those actively engaged in cancer research. Institutions making application are required to show that construction is needed for more effective cancer research by the key scientific staff already employed, that the amount needed for construction is substantial when measured against available and potential resources, that every effort has been made without success to secure matching funds, and that the cost of the proposed construction is reasonable.

Processing of the applications is similar to that for cancer research grants. They will be reviewed by staff members, consultants, and the National Advisory Cancer Council. Awards will be made by the Surgeon General of the Public Health Service with the advice of the Council.

New Institute laboratory-office building planned

The National Cancer Institute began study of its program plans as related to space requirements after $700,000 was provided in the 1961 appropriation for planning a new laboratory-office building. Institute program leaders and members of the Research Facilities Planning Branch, Division of Research Services, National Institutes of Health, are conferring with scientific and administrative personnel on information needed for drawing up architectural plans. The building will contain approximately 100,000 square feet and will permit expansion and consolidation of the intramural and extramural components of the Institute's research programs.

Friday, March 24, 1961.

NATIONAL HEART INSTITUTE

WITNESSES

DR. JAMES WATT, DIRECTOR, NATIONAL HEART INSTITUTE

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. LUTHER L. TERRY, SURGEON GENERAL

HARRY L. DORAN, CHIEF FINANCE OFFICER

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	3,979	5,108	5,353
	Positions other than permanent	70	75	91
	Other personnel compensation	49	45	30
	Total personnel compensation	4,098	5,228	5,474
12	Personnel benefits	537	633	685
21	Travel and transportation of persons	312	379	405
22	Transportation of things	61	75	84
23	Rent, communications, and utilities	83	81	82
24	Printing and reproduction	23	32	34
25	Other services	846	1,014	1,346
	Payment to—			
	"National Institutes of Health management fund"	3,790	4,163	4,633
	"Bureau of State Services management fund"	64	63	83
26	Supplies and materials	656	655	664
31	Equipment	527	230	243
41	Grants, subsidies, and contributions	50,071	73,643	77,624
	Total obligations	61,068	86,196	91,357

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	771	837	887
Full-time equivalent of other positions	15	17	21
Average number of all employees	637	742	787
Number of employees at end of year	743	807	901
Average GS grade	6.9	7.1	7.2
Average GS salary	$5,801	$6,358	$6,405

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(*a*) Research	35,907	55,073	61,420
(*b*) Fellowships	2,662	3,100	3,100
(*c*) Training	8,676	11,970	9,604
(*d*) State control programs	2,905	3,500	3,500
Total, grants	50,150	73,643	77,624
2. Direct operations:			
(*a*) Research	7,780	8 639	9,322
(*b*) Review and approval of grants	990	1,247	1,314
(*c*) Training activities	154	194	186
(*d*) Professional and technical assistance	1,493	2,313	2,622
(*e*) Administration	237	261	289
Total, direct operations	10,654	12,654	13,733
Total program costs	60,804	86,297	91,357
3. Relation of costs to obligations:			
Costs financed from obligations of other years, net (−)		−101	
Obligations incurred for costs of other years, net	265		
Total obligations	61,068	86,196	91,357
Financing:			
Comparative transfers to other accounts	497	704	
Unobligated balance lapsing	672		
New obligational authority (appropriation)	62,237	86,900	91,357

Mr. FOGARTY. The committee will come to order.

We have with us this morning the National Heart Institute. Dr. Watt, do you have a statement for the committee?

GENERAL STATEMENT

Dr. WATT. Yes, Mr. Chairman. I would like to submit it for the record, if I may.

With your permission, I would then like to summarize a few of the important developments.

(The statement follows:)

STATEMENT BY DIRECTOR, NATIONAL HEART INSTITUTE, PUBLIC HEALTH SERVICE

Mr. Chairman and members of the committee, a summing up of the year's activities of the National Heart Institute shows substantial progress.

The strengthened activities made possible this year have resulted in new and continuing investigations that are rapidly increasing research knowledge and opening new frontiers for exploration.

In the application of knowledge to control heart disease, community heart programs have developed more this year than in any previous year.

These programs have demonstrated outstanding benefits to individuals and to the community by providing services to heart disease victims in cooperation with their physicians. Methods have been tested which can be applied widely. Development of these services, such as those brought to the patient in his home, helps heart disease victims and reduces the burden they place upon hospitals, nursing homes, and other community resources.

In the control of heart disease and in research, new opportunities for still greater progress await the National Heart Institute as a consequence of the enlarged scope of its activities during the year.

HIGHLIGHTS OF RESEARCH ACCOMPLISHMENTS

Research progress made during the year, as evidenced by the hundreds of technical papers reporting results that were published in scientific and medical journals, has been impressive quantitatively and qualitatively. Advances were made on many fronts—in developing research methodology, in enlarging understanding of cardiovascular phenomena, in improving therapy of cardiovascular diseases, and in other areas. Some research accomplishments of particular interest are the—

recent finding by Heart Institute scientists that there are reflexes, originating in the sinus—hollow space or dilated areas—of the neck artery which controls the force with which the receiving chambers of the heart pump blood into the ventricles, thus importantly affecting the heart's performance and output.

technique reported by NHI grantees of treating heart attack patients by using a cardiac catheter to inject the clot-dissolving enzyme, fibrinolysin, into their coronary arteries, thereby assuring high concentrations of the enzyme at the site of the obstructing blood clot.

new developments by Heart Institute scientists which have greatly extended the usefulness of gas chromatography: (1) an improved technique for analyzing fats labeled with radioactive carbon and (2) a special analytical column making possible the analysis of steroids.

method of closed-chest cardiac massage, originated by NHI grantees, which can effectively restore bloodflow in persons with cardiac arrest without requiring surgical exposure of the heart, and thus can be used anywhere the emergency occurs.

modification by Heart Institute investigators of a heat-sensing element so that it can be used to diagnose the abnormal flow of blood through holes—caused by congenital heart disease—in the partition separating the two sides of the heart. The NHI method measures the concentration of previously injected cold saline in a blood vessel "downstream" from the heart. The new method eliminates the necessity of withdrawing large blood samples which are required in usual methods involving the use of dye solutions.

findings from NHI grant-supported studies of seven different animal species that the arachidonic acid content of serum cholesterol esters is highest in those species most resistant to atherosclerosis, suggesting that arachidonic acid deficiency may be a significant factor in development of the disease.

design of new and improved artificial heart valves, by both NHI and grantee investigators, and development of surgical procedures for installing them as replacement for severely damaged natural valves.

findings by NHI scientists that the liver is the source of the protein as well as the lipid fraction of lipoprotein molecules, which carry most of the fats in the blood.

first successful kidney transplant between nonidentical twins, an achievement by NHI grant-aided investigators who used whole-body irradiation to modify the recipient's immune response which would otherwise have caused rejection of the grafted kidney and its death.

findings by Heart Institute investigators that the mechanism by which the drug MER–29 (Merrell) lowers blood cholesterol levels is by blocking the last step in the chemical sequence by which the body manufactures cholesterol—and that this results in an increase in the body of its precursor, desmosterol.

development and successful use by NHI grantees, in treatment of patients with complete heart block, of a transistorized portable, artificial pacemaker, which is strapped to the patient's chest and maintains the heartbeat until his heart can resume normal rhythm.

evidence from Heart Institute experimental studies indicating that the interplay of the rates of deposit and removal of cholesterol from the artery wall is a major factor in the development of atherosclerosis.

findings of NHI-supported cooperative studies conducted in eight hospitals that large doses of the steroid, prednisone, and therapeutic doses of aspirin were both effective in controlling acute rheumatic fever symptoms in most patients and that neither was superior in preventing residual heart damage following rheumatic fever attacks.

effective technique devised by NHI grantees for closing small arteries (from which atherosclerotic deposits or blood clots have been surgically removed) by suturing the edges of the incision in the artery to a dacron patch rather than to each other, thus overcoming the constriction of the inner diameter of the artery that has been a grave hazard during healing after such operations.

findings of Heart Institute studies indicating that certain compounds that inhibit the enzyme monamine oxidase or the enzyme decarboxylase hold promise both as research tools in hypertension and as therapeutic drugs for treatment of the condition.

HIGHLIGHTS OF PROGRAM ADVANCES

Substantive areas of research both affect and are affected by developments of a programmatic nature.

Program mechanisms, therefore, are closely linked with substantive research, and program advances provide another insight into the year's progress. A few highlights from fields of particular interest show the kind and range of developments:

Cardiovascular drugs.—The encouragement of collaborative efforts with industry is resulting in such developments as (1) conferences on clot-dissolving agents that are clarifying problems and indicating that one outstanding need is for standardizing methods of drug preparations; (2) a cooperative clinical study to compare the efficiency of heparin and warfarin in treatment of myocardial infarction during the first month after an acute attack; and (3) recent publication of an index handbook on cardiovascular drugs covering some 13,400 scientific articles—a milestone and invaluable source of information in this complex field.

International activities.—Institute participation is growing and includes (1) increasing the interchange of scientific information—taking part in 10 international conferences on such subjects as primate research, gerontology, clothing agents, hypertension; (2) joint studies of several kinds, as, for example, between U.S. investigators and those of four other countries on the relationship of diet to coronary heart disease; and (3) a general burgeoning of scientific work, between scientists here and those abroad, in the cardiovascular field, expressed through growth in international heart research, training, and allied activities.

Diet studies.—The relationship of diet to heart disease, particularly coronary disease, is one of great public and professional interest: (1) the Institute, deeply concerned in this field, is vigorously supporting and conducting research in it; and (2) the rate and volume of research in this program area have grown this year.

Primate research resources.—The primate center program shows encouraging progress, such as (1) awarding of support for the construction and staffing of the first regional center (in Oregon) where work is well underway to implement it; and (2) increased interest in developing further primate centers evidenced by the number and quality of applications from major institutions in various parts of the country.

Heart clinical research centers.—Progress has been made in the relatively few months since this program's inception, so that (1) some 40 new applications for support of heart centers will be received and evaluated this year; (2) applications already in hand for National Advisory Heart Council consideration show thoughtful planning and strong interest on the part of the submitting institutions; and (3) the view is developing on the part of institutions that the centers will not only mean comprehensive research of a kind not heretofore possible, but also a partial aid toward stabilizing continued research activities.

Communications-education-information.—New efforts and substantial program planning are underway, supported by the National Advisory Heart Council and recognizing the interest of Congress, scientists, physicians, health workers, and the people in these important fields. The Institute is exploring and developing (1) communications research to aid scientists in keeping abreast of rapidly developing research, as exemplified by early implementation of collaborative work with the National Library of Medicine for a cardiovascular communications project; (2) professional education and ways to support the rapid bringing of new medical knowledge to physicians and nurses particulary (to help overcome the lag between research knowledge and its application), with an example of especial need constituted by a project endorsed by the Heart Council to implement a new educational effort to aid nurses; and (3) information plans, activities, and materials to provide comprehensive reporting on the Institute's programs, increased public information on heart research, and adequate health information and education for individuals concerning heart disease.

Training programs.—More than 300 graduate and undergraduate training programs are presently being supported, covering a wide spectrum which embraces (1) fellowships encouraging development of specialized skills and stabilization of careers; (2) training programs in institutions where there is high competence in the testing of cardiovascular therapeutic agents; (3) undergraduate training grants to 103 medical schools, schools of osteopathy, and schools of public health; and (4) support of graduate training in basic, clinical, combined clinical-basic, and developmental research areas.

STATISTICAL PICTURE OF HEART DISEASE

The size of the problem that research and control programs are tackling can be seen in the statistical picture of mortality from heart and blood vessel diseases.

The facts show that—

898,000 lives were taken in 1959 by diseases of the cardiovascular system.

474,000 of these deaths were from "heart attacks," or arteriosclerotic heart disease which involves them.

191,000 died in 1959 from blood vessel diseases of the brain, including "strokes."

81,000 deaths were caused by hypertension—sometimes with, sometimes without, accompanying heart disease.

18,000 died because of rheumatic fever and rheumatic heart disease.

Thus, diseases of the heart and blood vessels continue to account for more than 1 out of every 2 deaths that occur each year in the United States from all causes.

HEART INSTITUTE RESEARCH

The research conducted by the National Heart Institute places major emphasis upon basic cardiovascular investigations. These studies seek new knowledge about the structure, function, and abnormalities of the cardiovascular system. Closely associated with these studies are those concerned with the application of fundamental knowledge to the diagnosis, prevention, and treatment of diseases of the heart and blood vessels. Some Heart Institute accomplishments in these two areas are described below.

Atherosclerosis

During recent years laboratory studies on animals and epidemiological studies on human populations have amassed a body of evidence linking the development of the artery-clogging lesions of atherosclerosis to high blood levels of fatty substances, especially cholesterol. The amount and kinds of fat in the diet appear to influence the blood lipid picture, and may retard or accelerate the formation of these lesions. Their chief underlying causes, however, appear to lie somewhere in the complex process by which dietary fats are transported, synthesized, stored, or broken down by the body. Therefore, studies aimed at clarifying these processes of lipid metabolism and the mechanisms by which they are controlled continue to receive the major attention of intramural research in this disease area.

Cholesterol.—High levels of cholesterol in the blood, the factor most consistently associated with proneness to atherosclerosis, have been reduced in many cases by diets low in cholesterol and total fats, high in protein, and with a higher ratio of unsaturated to saturated fats. Although the cholesterol-lowering effects of unsaturated fats have been verified in many studies, the mechanism involved remains a mystery. Scientists of the NHI Laboratory of Cellular Physiology and Metabolism are collaborating with a researcher at the University of Lund, Sweden, in a study to determine whether unsaturated fats may increase the production of bile acids, an important mechanism for cholesterol excretion.

Although dietary measures may be beneficial in many cases, they are not likely to be the ultimate answer to the problem of preventing atherosclerosis. The body, especially the liver, readily manufactures cholesterol from acetate arising from the metabolism of fats, proteins, or carbohydrates, and even appears able to maintain excessive blood cholesterol levels when the diet contains no cholesterol. Thus, in recent years, an intensive search has been underway for nontoxic compounds that can reduce serum cholesterol by interfering with its synthesis.

Theoretically, cholesterol production can be blocked at any of a number of the biochemical steps by which the cholesterol molecule is formed. But blockade of a step too early in the process might also seriously compromise the synthesis of fatty acids, steroids, hormones, and other vital metabolites, while blockade of very late steps might lead to the accumulation of foreign sterols possibly more atherogenic than cholesterol.

Scientists of NHI and NIAMD have shown that one such compound, MER–29 (Merrell), lowers cholesterol by inhibiting the conversion of desmosterol to cholesterol, the last biochemical step of cholesterol synthesis. The fall in serum cholesterol levels observed in patients treated with the drug, however, was accompanied by a rise in serum desmosterol, so that total serum sterols were little affected in some patients and were actually increased in others. Much more must be learned about the biological functions of desmosterol before any accurate assessment can be made of the clinical value of this drug.

A promising approach now under study in the NHI Laboratory of Chemical Pharmacology is blockade of reactions involved in the conversion of mevalonic acid to squalene. This step in the synthetic pathway of cholesterol occurs far enough down the pathway so as not to interfere with other vital metabolic pathways requiring the same intermediate compounds. At the same time, it occurs early enough to avoid the potential problem of precursor sterol accumulation. Preliminary studies have shown that several compounds can block this step, but their effects have not yet been evaluated in laboratory animals.

Fatty acids.—Fatty acids are stored in the liver or in adipose tissue chiefly in the form of triglycerides, neutral fat resulting from the combination of three molecules of fatty acid with one molecule of glycerol.

These fat depots are not static: fatty acids are continuously being mobilized to meet the body's energy requirements at the same time that other fatty acids are entering the depots for conversion to triglycerides. These processes operate under the control of the endocrine system and are also subject to some degree of control by the autonomic nervous system. The mechanisms involved are therefore important determiners of blood lipid levels and may also figure importantly in atherosclerosis.

Studies completed this year in the Laboratory of Cellular Physiology and Metabolism have disclosed the probable sequence of steps by which triglycerides are formed in adipose tissue. Noting that the rate of fatty acid release from this tissue appeared to be closely related to the rate of triglyceride synthesis, the scientists also explored the possibility that hormones might trigger fatty acid release by inhibiting triglyceride synthesis rather than by promoting triglyceride breakdown.

The subsequent finding that triglyceride synthesis was strongly inhibited by glucagon, ACTH, epinephrine, and norepinephrine—four hormones which stimulate fatty acid release—provided strong support for this hypothesis. The studies also suggested that these four hormones affect fatty acid release by a common mechanism, but were unable to determine its nature.

Animal studies carried out in the Laboratory of Chemical Pharmacology have shown that various "stresses" such as prolonged exposure to cold result in excessive secretion of ACTH, which in turn triggers the release of other fat-mobilizing hormones from the adrenal glands.

Oddly enough, very similar "stress" responses can also be produced in animals by large doses of the depresssant, alcohol, and by sedative doses of the "antistress" drug reserpine. The excessive mobilization of fatty acids resulting from alcohol appears to be controlled in part by the autonomic nervous system, since this response could be blocked by drugs that inhibit the sympathetic division of this dual system. The "stress" responses to reserpine could also be blocked by monoamine oxidase inhibitors, usually thought as "psychic energizers" rather than as "antistress" drugs.

Lipoproteins.—Lipoproteins are fat-protein complexes that serve as transport vehicles for nearly all of the body's lipids. The distribution of lipids, especially cholesterol, among the various classes of lipoproteins also appears to be an important factor in atherosclerosis, abnormally high concentrations of cholesterol in the low-density lipoprotein fraction being associated with relative proneness to the disease. The ability of estrogens to shift the cholesterol concentrations of lipoproteins toward the higher density classes appears responsible for their protective effects.

The chief site of lipoprotein synthesis appears to be the liver, which has been shown by scientists of the Metabolism Section to provide both the lipid and protein fractions of the lipoprotein molecule. The studies also suggested that the rates of lipoprotein and cholesterol synthesis are independent of one another, and that overproduction of lipoproteins might be an important factor in the excessively high blood lipid levels found in nephrosis. Other studies showed that infusions of the protein albumin shifted the abnormal blood lipid patterns of nephrosis toward normal.

Studies on the mechanism by which cholesterol enters the arterial wall provide evidence to support the filtration theory of atherosclerosis, which holds that lipoproteins carrying cholesterol enter the arterial wall from the plasma, become trapped, and give rise to the lesions of atherosclerosis.

This study, conducted by scientists of the Clinical Endocrinology Section, indicated that the interplay of the rates at which cholesterol enters and leaves the arterial wall is a prime factor in the development of atherosclerosis. Factors which might influence these rates are under further study.

Gas chromatography.—Developed in England in 1952, gas chromatography—a method of separating a mixture into its specific chemical parts—has helped solve many problems of lipid analysis that had previously hindered research in this important field. Two important contributions made this year by NHI scientists have greatly expanded the scope of gas chromatography, extending its usefulness into heretofore inaccessible research areas.

One development, resulting from work done in the Laboratory of Technical Development, is an improved technique for using gas chromatography in the analysis of fatty acids labeled with radioactive carbon. This advance should greatly facilitate research on lipid metabolism, in which radioactive tracers are often used to follow the metabolic fate of fats in the body.

The other, from the Laboratory of the Chemistry of Natural Products, makes possible the use of gas chromatography for the analysis of steroids, a large family of compounds which includes cholesterol, several vitamins, and many important hormones. The same technique has also been used successfully in the analysis of many alkaloids, an enormous group of plant substances which, in the past, has yielded many important drugs.

Hypertension

The underlying cause or causes of hypertension remain obscure. Though it has not been demonstrated that amines—organic compounds containing nitrogen—are themselves culprits in its cause and development, it is abundantly clear that many drugs which alter amine metabolism also effectively lower blood pressure in hypertensive patients. For these reasons, the research program on hypertension is continuing to concentrate its efforts on obtaining a more complete knowledge of the processes of amine metabolism.

The studies cited below were carried out in the Laboratory of Chemical Pharmacology, the Laboratory of Clinical Biochemistry, and the Laboratory of General Medicine and Experimental Therapeutics.

A large number of amines are manufactured by the body from the amino acids of dietary protein. The two which appear to figure most prominently in the effects of a number of drugs used to lower blood pressure are norepinephrine and serotonin. One of the functions of the norepinephrine is that of a sympathetic neurohormone: sympathetic nerve impulses trigger the release of norepinephrine at the nerve terminals, and this amine then transmits the stimulus to the muscles of the blood vessel wall, causing constriction of that vessel.

If the action of this amine is blocked in some manner, the vasoconstrictive response is prevented as effectively as if the nerve itself had been cut, with the important difference that the drug effect is temporary and controllable.

Most compounds currently in use to reduce blood pressure owe their effects on blood pressure to such a "chemical nerve cutting," although they might differ considerably in their mechanisms of action. Some appear to prevent the release of norepinephrine in response to nerve stimuli; others to block its production; and still others to prevent the amine from being stored at its site of action, thus effectively depleting the nerve terminal area.

Studies at NHI have shown that the sedative and tranquilizing effects also produced by certain of these drugs are owing to their action on another amine, sterotonin. Reserpine, for example, produces its sedative and tranquilizing effects by depleting brain serotonin stores. This action of these drugs is not related to their effects on blood pressure, and the resulting effects are often undesirable in the therapy of hypertension. Thus the search has continued for drugs that will block the action of norepinephrine peripherally, but will not affect brain amines.

NHI studies have revealed that Syrosingopine (Ciba), made by modifying the reserpine molecule slightly, is an improvement over reserpine in that it retains its selective action on peripheral norepinephrine over a much wider dosage range.

However, guanethidine (Ciba), a drug that differs chemically from reserpine and its analogs, is even more specific. The drug effectively lowers blood pressure by a still unclarified action on peripheral norepinephrine, but has no effect on brain amines. This appears to be due to the drug's inability to penetrate the blood brain barrier. This drug appears to meet a number of criteria for the "ideal hypotensive agent."

A promising new family of compounds now undergoing clinical trials at NHI are decarboxylase inhibitors. These inhibit the synthesis of several amines, including norepinephrine and serotonin, by blocking the action of decarboxylase, an enzyme necessary for the production of these amines from amino acids.

The first of these compounds studied was alpha-methyl DOPA (Merck Sharp & Dohme), which has been found to lower blood pressure in hypertensive patients. At first it appeared that the drug's hypotensive action was due to its inhibition of norepinephrine synthesis. However, evidence is accumulating to suggest that its action is more complex. Animal studies, and certain clinical observations indicate that the drug might also exert a sustained action on norepinephrine storage similar to that of reserpine, but far more specific for that amine.

Much further research will be required for a full evaluation of alpha-methyl DOPA and its relatives. Their potential at this time appears to be excellent both as research probes in studies on amine metabolism and as possible therapeutic agents.

Another family of enzyme inhibitors, the monoamine oxidase (MAO) inhibitors, continues to be investigated by NHI scientists. These compounds, which block the action of MAO, an enzyme that inactivates a number of amines, lower blood pressure by a mechanism still incompletely understood.

Several of these compounds previously tested were potent hypotensive agents, but were too toxic for therapeutic use. A new compound undergoing limited clinical trials shows promise of being equally effective in lowering blood pressure. It also appears, so far, to be largely free of toxic effects. This drug, MO–911 (Abbott), differs markedly from MAO inhibitors previously tested in its chemical structure.

Congestive heart failure

The heart is a very complex, highly sophisticated pump which provides the driving force for an equally complex and sophisticated system of plumbing. This system exists to take up and transport oxygen, nutrients, and other essential substances to the cells making up the body tissues and organs, and to take up and transport the waste products of cellular metabolism to the sites of their disposal. The demands of these tissues fluctuate widely. Since the heart is the servant of the tissues rather than their master, numerous nerve and hormonal pathways exist for modifying heart output in accordance with these changing needs. Although these pathways are numerous and their mechanisms varied, their resultant effect on heart output is expressed in only two ways: (1) changes in the number of pumping strokes per minute and/or (2) changes in the amount of blood ejected with each pumping stroke.

Factors affecting heart output.—Heart output per unit time can be increased by increasing heart rate alone, but only up to a point. After this, cardiac pumping efficiency falls off so rapidly that further increases in heart rate actually reduce heart output. Heart output can also be increased by increasing the pressure at which the heart is filled.

The Frank-Starling law, sometimes called merely Starling's law, for many years the basis for explaining the response of the heart to carrying loads, states that increased filling pressure increases the length of the heart muscle fibers, causing a more vigorous contraction of those fibers and increased heart output. However, this increase is also effective only up to a point. Beyond it further lengthening does not produce further increases in heart output, and in fact, leads eventually to reduced output.

The Frank-Starling law has been the subject of an important series of studies by scientists of the NHI Laboratory of Cardiovascular Physiology. Their work has shown that the Frank-Starling relationship is continuously operative, but is also continuously subject to modification as the result of stimuli from either the excitor (sympathetic) or depressor (parasympathetic) divisions of the involuntary nervous system or from norepinephrine and other related amines. These factors importantly influence heart output by—

(1) causing the heart muscle fibers to contract more or less forcefully from any given fiber length;

(2) causing the heart's receiving chambers (atria) to contract more or less forcefully, thereby modifying ventricular filling pressure and ventricular fiber length; and

(3) affecting the timing of the sequence of events in the cardiac cycle

These findings have been integrated into "the principles of the innervated heart," which greatly extend the scope of the Frank-Starling relationship. These also help to clarify the means by which the central nervous system can produce acute changes in heart performance other than by affecting heart rate.

The carotid sinus is the dilated portion of the carotid artery in the neck and is the site of many nerve pathways. This sinus has long been known to react to changes in arterial pressure by initiating nervous reflexes to modify heart rate and peripheral resistance to blood flow.

NHI scientists have found that this pressure receptor initiates still another set of reflexes which importantly influence ventricular performance and heart output by controlling the vigor of atrial contraction.

When arterial pressure falls, the carotid sinus reflexly diminishes the activity of the vagus nerve (which normally restrains the pulse of the atrium or receiving chamber of the heart) while simultaneously increasing the activity of the cardiac sympathetic nerves. Sympathetic stimulation increases heart levels of norepinephrine, causing the atrial muscle fibers to contract more forcefully from any given filling pressure and fiber length. The sharper, more vigorous atrial contraction pumps more blood into the ventricle, elongating its muscle fibers more than would otherwise occur.

The increase in ventricular fiber length (which is combined with a similar direct response of the ventricular muscle to the sympathetic stimulation) causes a more vigorous ventricular contraction and increased heart output. The effect of parasympathetic stimulation may be further augmented by amines from the adrenal glands.

However, when arterial pressure is high, the carotid sinus reflexly decreases sympathetic activity and increases vagus activity. Vagus stimulation does not affect the ventricle directly. But it does suppress the atrial pulse and reduce the contribution of the atria to ventricular filling, and results in reduced output.

Norepinephrine and sympathetic stimuli also contribute to cardiac efficiency by their effects on the timing of certain events in the cardiac cycle. Both shorten the duration of atrial and ventricular contraction in addition to increasing their vigor. This effect becomes increasingly important at higher heart rates by affording more time for adequate atrial and ventricular filling, without which cardiac efficiency falls off sharply.

Digitalis and related compounds.—Digitalis and other related compounds have been used for many years to augment heart output in congestive heart failure. The pharmacology of these drugs has been studied by scientists of the Surgery Branch and their effects on the failing and nonfailing heart evaluated.

The studies showed that these drugs increased the contractile force of the failing and nonfailing heart; however, heart output was not increased proportionally. This discrepancy appears to be caused by the potent blood vessel constrictive action of these drugs. As a result, though the contractile force of the heart is increased by the drugs, so also is the resistance against which the heart must work. Thyroid hormone was found to antagonize the action of these compounds. This antagonistic action appears to be mediated by norepinephrine and related amines, since reserpine, which depletes the tissues of amines, also blocked the antagonistic effects.

Aldosterone.—Aldosterone, a hormone from the adrenal cortex, is charged with an important role in the maintenance of blood volume and hence blood pressure. The release of aldosterone results in increased retention of salt and water by the kidneys and also by other organs such as sweat glands. However, excessive alderstone secretion also frequently attends congestive heart failure, and contributes to the edema that often accompanies this disorder.

Hypersecretion of aldosterone can readily be produced in animals by measures which reduce blood volume or blood pressure. However, the immediate stimulus to aldosterone secretion appears to be still another hormone. The source of the hormone which stimulates aldosterone secretion and the mechanism or mechanisms governing its release have been the subject of much research and much conflicting evidence.

Recent studies in the Laboratory of Kidney and Electrolyte Metabolism indicate that the hormone is not secreted by the pituitary or any other intracranial structure previously suspected of being the site of its production and secretion. On the other hand, the study has provided strong evidence that the hormone is produced by the kidney.

Surgery

A major area of research in the NHI Surgery Branch is the development of techniques and procedures for more precise diagnosis and localization of congenital and acquired heart defects and for more accurate evaluation of their magnitude. The more accurate these data, the more precisely the surgical team can plan its procedures to make maximum use of the very limited time available when the patient is being operated on. The team can anticipate and plan for difficulties that may arise. Thus, too, they can provide maximum benefit to the patient while minimizing the risk that inevitably atends heart or any other surgery.

Several new procedures have been shown by clinical studies to be highly reliable sensitive means for detecting, localizing, and estimating the magnitude of cardiac shunts.

A shunt is the flow of blood through abnormal openings in the partition separating the left and right sides of the heart.

One such procedure involves the injection of radioactive krypton into the heart by a cardiac catheter. A left-to-right shunt can be detected by injecting the krypton into the left side of the heart, then monitoring the radioactivity of the air exhaled by the patient.

Right-to-left shunts are detected by injecting the krypton into the right side of the heart, drawing blood samples from a systemic artery during the next 15 seconds, and measuring their radioactivity. Since nearly all of the krypton should be eliminated in the lungs before entering the systemic arteries, its presence in these blood samples means that it must have crossed directly to the left heart via a right-to-left shunt.

Indicator dilution curves have been used for several years to detect shunts. In this technique, the indicator (usually dye) is introduced into the appropriate side of the heart. Its concentration is subsequently measured in blood from an artery directly downstream from that side of the heart. This blood is slowly drawn at a constant rate. As it enters the syringes the dye concentration is continuously measured and recorded. Normally, these concentrations plot as a curve with a sharp upslope, folowed by a smooth, gentle downslope. However, a shunt causes a second peak, as dye detoured by the shunt to the other side of the heart now makes a delayed appearance.

Although it is a reliable method of diagnosis, the method requires withdrawal of rather large blood samples and frequently necessitates transfusions, especially in small children.

The work of other scientists had demonstrated the applicability of two other methods for diagnosing shunts, neither requiring withdrawal of blood samples. Using this work as a basis, NHI scientists have modified and refined the techniques and instrumentation used in these methods, and have used both of them successfully in a number of clinical cases.

One method uses ascorbic acid (vitamin C) as the indicator, which is injected in the same way as described previously for dye. The major difference is that ascorbic acid concentration in the arterial blood downstream can be continuously measured by a small platinum electrode inserted into the artery by a needle or catheter. The electrode carries a small positive charge, applied from a low-voltage direct current circuit. Ascorbic acid molecules coming into contcat with the electrode give up electrons, producing an increase in the circuit voltage that is proportional to the concentration of the ascorbic acid. This is recorded and evaluated in the same way as the dye concentration curve.

The other method uses cold saline solution as the indicator, and measures its concentration with a heat-sensing element called a thermistor. The changes in temperature produced by the indicator are analogous to the changes in concentration of injected dye or ascorbic acid.

Other important studies have been directed toward the development of new, improved artificial heart valves and synthetic replacements for severely diseased arterial segments, and toward perfecting surgical procedures for their successful installation.

The heart valve most often damaged by rheumatic fever is the mitral valve—a two-lipped valve called mitral because it looks something like a bishop's miter. This valve lies between the upper receiving chamber and lower chamber of the heart's left side.

An artificial mitral valve, very similar in structure to the normal mitral valve, has now reached the stage of clinical trial. It shows great promise in the treatment of mitral insufficiency that cannot be corrected by other surgical procedures.

Another artificial valve has been designed to replace the pulmonic valve lying between the right ventricle and the pulmonary artery to the lungs. The valve and the technique for installing it have been tested in animal experiments, and both appear promising.

Studies now in progress are designed to determine the best combination of prosthetic materials and installation techniques to overcome the formidable problems of pulmonary artery replacement. The low pressure in this vessel, when coupled with its lack of any adjacent supporting structures, makes any prosthetic replacement subject to kinking. If these problems can be overcome, several congenital defects not now correctible may become amenable to surgery.

In choosing the best synthetic material for use in a particular artificial valve or arterial prosthesis, the scientist today is confronted with a bewildering array of materials which differ considerably in their flexibility, wettability, tendency to acqure static charge, and surface characteristics.

Of particular concern in the choice of synthetics are those properties of a particular material which might either promote or inhibit the formation of blood clots. NHI scientists have studied and evaluated some of these properties in 30 different synthetic materials that are currently available.

Their studies showed that the relative tendency of such materials to promote or inhibit clot formation was determined more by the chemical nature of the surface than by its wettability or electrical charge. Surfaces with highly negative static charges or surfaces which acquired such charges by chemical interaction with charged chemical radicals appeared to be the best inhibitors of clot formation.

Investigations are continuing to find materials which will meet criteria for safe use when placed in human beings.

Gerontology

What happens to the heart, blood vessels, and blood as man grows old affects life and health in the whole body and its every cell more than happenings in any other of man's organ systems. The National Heart Institute's concern with gerontology stems from the fact that the aging process is thus inextricably tied to the phenomena of the cardiovascular system.

The Gerontology Branch of the Heart Institute is seeking answers to three knotty questions: (1) What is aging? (2) Why does it occur? and (3) Is aging an inexorable process or can it be retarded or else modified to minimize loss of vigor and capability with aging? The research program encompasses many scientific disciplines. The scope of studies ranges from observations on the whole animal to studies on specific organ systems and tissues and to the exploration of cells and their components.

The animals studied extend from single-celled protozoans through primates. The simplest animals, such as protozoa and coelenterates, are especially useful in studies on age modifications in cellular phenomena or in the functions of simple organ systems. Age changes in more complex systems and the role of genetics in aging can be studied advantageously in intermediate animals such as insects, whose short lifespans also permit observations to be made from birth to death. The study of aging in higher animals, while more complex and difficult, provides data on physiological systems more similar to those of man.

Studies on man.—The primary concern of the Gerontology Branch, however, is to learn more about aging and its physiological and psychological ramifications in man. And though many questions about aging might be answered by animal studies, many of the most important ones can be answered only by studies on humans.

Of necessity such studies have been confined largely to observations on aged subjects in hospitals, nursing homes, or homes for the aged. These people might fairly be expected to present more than the average number of abnormal findings, both physiological and psychological. This probability to some extent affects the validity and limits the range of data gained from these studies. To avoid a distorted picture and to gain a wider range of data, more studies are needed to older people who still occupy their niche in the family and in the community

The Gerontology Branch is fortunate enough to have one of the very few such groups of subjects for study. This group consists of men 24 to 99 years old who are still active in family and community life. They have volunteered to spend 2 days in the laboratory every 18 months for the rest of their lives.

During their laboratory stay, they participate in the entire series of standardized tests. These include functional evaluation of the lungs, kidneys, cardiovascular system, and muscular system; estimation of body composition, basal metabolism, neuromuscular function, and response to exercise; and a battery of psychological and personality tests.

Studies on this group have helped to refute the notion that aging must inevitably be accompanied by rapid deterioration and disease.

New "normal" standards developed.—Even more significantly, however, they have provided more accurate indices of what constitutes "normal" physiological and psychological performance in older people. They have also led to the development of standardized tests and procedures that provide more accurate measures, than have heretofore been available, of performance when applied to older people in general. "Normal" standards for older people are essential for distinguishing between changes resulting from aging and changes caused by disease. Most of the standards previously used had been worked out on young, normal adults, chiefly medical students.

New standardized tests and procedures developed by the Gerontology Branch are presently being adopted by many gerontologists in this country and also by many gerontologists abroad.

In addition to their greater validity, the data gained from studies using these procedures can be compared with that from any other study in which they were used, which greatly enhances the value of such data.

As a science gerontology is emerging from that first stage through which any new science must necessarily pass: a period of great promise but limited achievements, of seeking parameters to measure and for means of measuring them, of recording aging phenomena without finding out why they occur, of establishing criteria rather than applying them.

Now the foundation has been laid and the framework erected for the second stage: a period of gathering data in accordance with established working hypotheses; of data comparison and evaluation; of fitting isolated bits and pieces into a more complete and comprehensive picture of the physiology of aging; and of the application of this knowledge, integrated with the socioeconomic aspects of aging, for the benefit of our rapidly growing geriatric population.

Growth and needs of gerontological research.—During the first stage, the NHI Gerontology Branch provided much-needed leadership. Such leadership will be even more essential as the full growth of gerontology comes about.

The Gerontology Branch was begun as a small research unit of NIH in Baltimore nearly a score of years ago. It has become an integral part of community and State life through the years. It has worked in partnership with their medical and scientific institutions and civic organizations.

An example of the close relationships between State agencies and the Gerontological Branch is afforded by the activities of the Maryland Commission on Aging, which has held meetings at the branch and at the Heart Institute in the past year. There have also been working relationships with health and other agencies, public and private.

Such cooperation has benefited both parties: the State by the availability of branch facilities for use in connection with the program, and the Gerontology Branch by the availability of large numbers of subjects for study. The Gerontology Branch thus constitutes a unique research institution in gerontology. As has been said, "There is nothing like it in the United States; it represents a research enterprise that has played an indispensable role in research progress in aging."

RESEARCH GRANTS

The research grants program of the National Heart Institute supports heart disease research in over 300 universities and hospitals all over the country. More than 2,000 separate research projects are currently underway.

Here are a few of the new findings from research projects in arteriosclerosis, hypertension, rheumatic fever and rheumatic heart disease, cerebrovascular disease, and cardiac emergencies.

Arteriosclerosis

The differing susceptibilities exhibited by various animal species to atherosclerosis may be related to the composition of their serum lipids. Information derived from studies on different species, therefore, is important to the medical research field.

According to a study on the serum cholesterol ester fatty acids in eight species of birds and mammals, the outstanding variation was the proportion of arachidonic acid in this serum fraction. The rat and dog with high levels are highly resistant to the development of atherosclerosis. The goose, chicken, rabbit, and pig with low levels are known to be susceptible to the induction of atherosclerosis, whereas the levels in humans are somewhat intermediate. This suggests that the level of arachidonic acid in the cholesterol ester fatty acids may be related to susceptibility to atherosclerosis. However, it remains to be determined if the proportion of arachidonic acid in this serum fraction is a species characteristic or if it and the susceptibility to atherosclerosis can be altered.

A 5-year longitudinal study of a lower middle income group of persons living in New York City indicates that serum cholesterol levels change with age. In general, females show a preadolescent decrease, a post adolescent increase, and a noticeable increase after age 35, whereas males show a preadolescent decrease and a postadolescent increase of less magnitude than females, and a sharp increase from ages 20 to 40 with constancy after 40. These findings tend to support the view that coronary artery disease, which tends to afflict men at an earlier age than women, is correlated with prolonged hypercholesteremia.

Among the further indications of hormonal influences in atherosclerosis is the effect claimed for certain extracts of the anterior pituitary gland that markedly raise the level of blood lipids of experimental animals within 12 to 24 hours following subcutaneous injection. Elevated levels of certain lipids are widely considered to be characteristic of individuals who subsequently develop clinical symptoms of atherosclerosis.

In another study extending over a 20-year period on female patients, a higher incidence of atherosclerosis occurred after bilateral ovariectomy (castration) prior to the menopause than occurred after hysterectomy without castration. The atherosclerosis manifested itself clinically as coronary artery disease and peripheral vascular disease. The incidence of hypertension and enlarged heart was also higher in the castrate group and even more pronounced in those with vascular disease.

Hypertension

A study of hypertensive subjects indicates that hypersecretion of aldosterone does not participate in the development of benign essential hypertension, but that in the pathogenesis of malignant hypertension significant to marked hypersecretion of aldosterone occurs in almost every case examined. This excessive adrenal output apparently is not due to a neoplastic growth in the adrenal. Further research is necessary in order to determine whether or not this hypersecretion plays a causal role in malignant hypertension.

Further insight into the still uncertain mechanism of chronic renal hypertension has resulted from recent experimental studies. They indicate that the persistence of elevated blood pressure following temporary restriction of the blood supply to the kidneys is not owing to substances liberated by the kidney which produce constriction of the arteries.

A new diagnostic test has been devised to differentiate primary hypertension from hypertension due to pheochromocytoma (tumor of adrenal medulla). Vanillylmandelic acid, a product of metabolism present in small amounts in the urine of normal subjects and patients with primary hypertension, has been detected in abnormally large amounts in the urine of all patients with pheochromocytoma.

Rheumatic fever and rheumatic heart disease

Advances have been made in understanding the relationship of recurrent rheumatic fever attacks to the development of lesions of the heart valves.

Studies on a large series of patients indicate that damage to the cardiac valves in susceptible patient usually occurs during the first rheumatic fever attack. If there are no valvular complications during the first attack, these patients for the most part do not develop rheumatic heart disease during subsequent attacks. These findings suggest that the rheumatic host has a persistent ability either to resist or to succumb to valvular involvement.

Further research must be done to see if antibiotic prophylaxis can be safely discontinued in the resistant group and to try to find out what it is in these people that provides them with resistance to repeated attacks of rheumatic fever.

Studies with group A hemolytic streptococci show that morphological variants of this organism can grow in the presence of penicillin. This inhibits growth of the original streptococci because of penicillin interference with formation of the bacterial cell wall. These variants without cell walls can nevertheless elaborate the toxic antigens and lysins characteristic of the parent type associated with rheumatic fever. Such findings are of interest in relation to the development of drug-resistant pathogenic micro-organisms.

The improvement of surgical procedures for the alleviation of rheumatic heart disease is under continuing study. One series of adult patients, undergoing surgical correction of calcific narrowing of the outflow tract from the left ventricle, shows an encouragingly low operative mortality rate. A high percentage of the survivors ½ to 3 years later were improved.

Open-heart surgery for acquired heart disease, such as valvular heart disease secondary to rheumatic fever, is still in the experimental phase. It is of proven value in selected cases with specific lesions.

For example, a followup study reveals that open-heart technics now provide a satisfactory means for correction of a disabling valvular insufficiency that causes regurgitation of blood between chambers of the left side of the heart.

Two types of artificial valves have been developed for the replacement of irreparably damaged aortic valves. One, a flap valve, has been inserted successfully in a small number of patients. The other, a bicuspid valve, is undergoing trials in animals. The valves are made of silastic, a rubbery silicone plastic, bonded to a polyvinyl sponge base. They are inserted through a slit in the aorta and secured by sutures at the site of the natural aortic valve.

CEREBROVASCULAR DISEASE

A cooperative study on extracranial arterial occlusion involving approximately a dozen different investigators is currently underway. The objective of this program is the improvement of diagnostic procedures and the selection of appropriate patients for surgical therapy for the relief of cerebrovascular insufficiency. A standard protocol has been developed to insure comparable results. New arteriography technics that demonstrate the patency or occlusion of cerebral vessels will be devised and correlated with electroencephalographic recordings.

Surgical techniques such as direct suture, grafting, and others have not been feasible intracranially owing to the limited size of the cerebral vessels and the difficulty in maintaining flow without thrombosis. A nonsuture method of small vessel anastomosis, applicable to both artery and vein, has been developed in animals. The techniques, when used in a variety of combinations, make it possible to perform arteriotomy, vessel reconstruction, grafting, and vessel anastomoses, with a high and reproducible incidence of success. Applicability to the problems of human intracranial vascular surgery awaits further animal experimentation, particularly long-term studies of the abilities of blood vessels to retain their open channels and the durability of the plastic bond material used in the operations.

The mechanism of brain swelling seen in the presence of changes in intrathoracic pressure is being defined more clearly. Experiments with dogs have revealed that respiratory obstruction during general anesthesia favors elevation of intracranial pressure, and under certain conditions, leads to hemorrhages in the veins around the outer layers of the brain.

A simple method of studying cerebral blood circulation, using radioactive-labeled red blood cells, has been devised. This method may prove valuable for detecting certain cerebrovascular diseases.

Cardiac emergencies

A method of external transthoracic cardiac massage has been developed which is of value in emergency cases of cardiac arrest. This method provides adequate circulation for the maintenance of the heart and nervous system and its use on 20 patients has given a survival rate of 70 percent.

Several cardiac pacemakers have been developed, including a portable model for treating complete heart block in patients. This model has maintained normal heart rhythm in patients for periods up to 15 months, until diseased or injured tissues regenerated and the heart's own pacemaker resumed maintenance of normal heart rhythm.

AREAS OF ESPECIAL INTEREST

Training

As the many facets of research in cardiovascular disease are explored and as methods and techniques become improved, more and better qualified people are required to carry on medical investigations. The National Heart Institute is currently supporting over 315 undergraduate and graduate training programs to help fill this need.

While preclinical, or basic research training is an integral part of the Heart Institute training program, clinical research training has been receiving particular emphasis.

This type of research training is patient oriented, dealing with experimental diagnostic and therapeutic techniques and the application of newer basic scientific knowledge as it applies to the pevention and treatment of diseases of man.

Included are such areas as medical and surgical cardiology, peripheral vascular disease, and clinical therapeutics. The study of clinical therpeutics or drug evaluation is of immediate concern to the Heart Institute. The adequate clinical trial of drugs as they relate to cardiovascular disease requires the employment of difficult and exacting methods and few qualified investigators are available to handle this important area of medical research.

Attempts are being made to increase the reservoir of experienced personnel in this field by establishing training programs at institutions displaying high competence in the testing of cardiovascular therapeutic agents.

The fellowship program continues to play an important part in the training activties of the National Heart Institute. Fellowship awards serve to encourage competent postdoctoral research workers to attain specialized skills in particular research areas in the heart field. Strengthening of the fellowship program has been possible this year because of the funds made available by the Congress.

The undergraduate training program, another aspect of the Institute's support of training, has enabled the schools to provide more comprehensive and intensive training in the clinical and public health aspects of cardiovascular disease. It has also helped stimulate and strengthen research in the schools. Many more medical students have become interested in medical research since it has been made possible for them to participate in the research activities of their schools. These beneficial effects of the undergraduate training grants will continue to be in force in the schools.

Graduate training grants support special training programs in basic and clinical cardiovascular research areas in medical schools, universities, and other training institutions. They help to provide greater stability to meritorious training programs in various basic and clinical disciplines in the cardiovascular field. This type of grant is an effective means of helping to produce research personnel in areas of manpower shortage. These programs aid in bringing the basic and clinical scientists together in broader study of cardiovascular diseases through training involving multiple disciplines and several departments. Training programs are utilized to establsh instruction in new or undeveloped disciplines to take advantage of unusual opportunities and new approaches.

Another goal of the Institute program has been to establish training in new areas where trained personnel are sorely needed.

For example, several training programs are being supported which are multidisciplinary, combining the engineering schools and medical school departments in an effort to train people who can utilize the techniques of the physical sciences in biological research.

The need is sizable for cardiovascular investigators thoroughly trained in electronics so that they can make full use of the great potential of this field in its relation to heart disease. This type of training will enable them to design telemetering devices, artificial pacemakers, and better diagnostic instruments.

for research and academic careers in fields closely allied to cardiovascular research and medical care. Training programs in nursing and social work are examples of this area.

Participation in international research

The National Heart Institute is supporting several investigations in foreign countries that are exploring national differences in various aspects of cardiovascular disease.

A joint study by scientists in the United States and the United Kingdom is attempting to determine the reasons for the marked difference in the mortality from chronic respiratory and cardiovascular diseases in the two countries. The death rate from coronary heart disease is nearly twice as high in the United States as in England and Wales. Respiratory diseases (such as bronchitis, emphysema, bronchiectasis, and pneumonia) cause about three times as many deaths in England and Wales as in the United States.

The increasing frequency with which those respiratory diseases have been reported as causes of morbidity and mortality in the United States in recent years makes a collaborative study especially timely.

Another cooperative study, one focused on the relationship of diet to coronary heart disease, is being carried on by investigators in the United States and in four other countries whose people have distinctly different dietary habits from us and from one another.

Another project abroad is a study of diet and heart disease among Chilean farmers. Thus study is comparing the diet of white people of Spanish extraction with that of native Araucanian Indians. It is also comparing heart disease occurrence and mortality in the two groups.

International meetings.—Considerable activity has developed in connection with international conferences. The Heart Institute has participated in or provided support for 10 productive international meetings which have taken place since April 1, 1960.

Three of these were held in this country—two on thrombolytic agents, one on gerontology. The other seven were held in such diverse locations as Prague, Melbourne, Rio de Janeiro, Leopoldville, Geneva, and Tokyo (2); and dealt with hypertension, cardiology in general, primate research, nephrology, hematology, and blood transfusion.

In all cases a special effort was made by the Heart Institute to foster the attendance and participation of young investigators as well as more seasoned individuals. As a result of personal contacts generated by these meetings, a growing stream of correspondence on subjects of mutual interest, as well as a lively exchange of scientific publications, is developing between our young scientists and those in other countries.

The support of the meetings in foreign countries was generally provided through a grant to some responsible American organization for the provision of travel expenses at a modest level. The bulk of the funds involved was thus spent as dollars in this country and went mostly for plane fares. A rise in the number and quality of research grant applications from foreign sources is expected as the result of (1) the increase of face-to-face scientific discussions between investigators at international meetings, and (2) the expansion of the foreign fellowships program.

Exchange missions.—A delegation of four Soviet scientists visited the Heart Institute in May of 1960 to participate in planning a joint program of scientific cooperation in the field of heart disease. A week of discussions with officials and consultants of the Heart Institute was followed by a week of visits to research institutions at Baltimore, Boston, and Cleveland. A discussion of plans for collaborative studies and the exchange of scientific personnel and information, held at the Public Health Service's regional office in New York, concluded the first exchange visit.

The meetings were considered highly fruitful by the two groups and several agreements were reached. Each party agreed (1) to prepare a list of subjects and areas in which they are particularly interested in exchanging workers, (2) to prepare material and suggestions relating to the nomenclature and classification of cardiovascular diseases, (3) to proceed with plans for the exchange of individual scientists, and (4) to expedite the exchange of cardiovascular journals, books, and films.

Later in the year, three members of the U.S. group met again with members of the Russian delegation, following the meeting of the Third European Congress of Cardiology in Rome. Discussions of information exchanges and possible cooperative studies were held. Further cooperation will be facilitated at a return meeting to be held in the U.S.S.R. during 1961.

Epidemiology, a developing tool

The potential of the epidemiological approach to cardiovascular disease begins to be realized as patterns of relationship emerge from painstakingly accumulated data. Studies (such as the long-term epidemiology study conducted by the Heart Institute at Framingham, Mass.) are being carried on to explore all of the various factors and influences which may contribute to the development of coronary heart disease.

From the mass of material, certain observations of considerable pertinence have been made. It has become clear that the level of the serum cholesterol is of potential importance as a predictor of future coronary heart disease. The higher the blood cholesterol level, the more likely is the later development of coronary heart disease, according to present epidemiological data.

Similarly, it is clear from epidemiological data that the higher the blood pressure, the more likely will be the early development of coronary heart disease.

Although overweight has long been accepted as contributing to the development of hypertensive and coronary heart disease, it is only now that this problem is being clarified. Epidemiological studies lend strength to the belief that overweight is a hazard. They suggest, however, that it may be through the mechanism of elevating serum cholesterol and raising blood pressure that obesity exerts its effect.

Additional evidence on the mortality and morbidity from coronary heart disease among smokers and nonsmokers has become available from three studies conducted by the Public Health Service. Male cigarette smokers experienced a significantly higher death rate from coronary heart disease and a significantly higher incidence of myocardial infarction than did males who never or only occasionally smoked cigarettes. This relationship was more marked among men in early adult life and also was found among males living in rural and urban communities. The higher incidence of myocardial infarction among cigarette smokers appeared to be in addition to the effects of elevated serum cholesterol, high blood pressure, and overweight.

The assessment of many other factors is being carried on in several other studies. These studies all indicate that the hope of being able to describe those who are at high risk of developing coronary heart disease is being achieved. If adequate methods of selecting the "coronary prone" person become available, then the application of preventive procedures, as they develop, can become more specific and practical.

Field epidemiology research.—The Heart Institute has a number of field studies currently underway which are seeking to identify factors of man and his environment that relate to the occurrence of specific disease.

At Memphis, Tenn., studies in progress are designed to identify differences in the kinds and amounts of cardiovascular disease between white and nonwhite populations.

At New York City, identification of factors associated with coronary disease are being sought through a study in which family members of individuals who died unexpectedly are interviewed regarding symptoms and activities preceding the sudden death.

A study being initiated at Columbus, Ga., will be concerned with the relationship of obesity and heart size to the cause and time of death.

The study population will consist of cohorts of city residents first examined during surveys in 1946 in Columbus.

At Rochester, Minn., a followup study of blood pressure levels (in individuals first examined in the 1930's) is being carried out in collaboration with the Mayo Clinic. This study will measure the incidence of hypertensive disease and the significance of the cold-pressor test as a predictor of subsequent abnormality.

Recent findings in grants research.—An epidemiologic study of Negroes in the Bahama Islands reveals a high prevalence of elevated blood pressure. Comparison of the findings with the results of previous studies of Negroes in the Virgin Islands and the United States suggests that the blood pressure of Negroes is higher regardless of the geographic area studied or level of civilization (primitive rural versus modern urban). High salt intake and familial factors may be involved in the prevalence of hypertension in this Bahama population. Additional dietary and genetic studies are being carried out in order to clarify the causes of this condition.

A gradient of decreasing mortality rates from coronary heart disease with increasing physical activity of work in middle-aged men has been reported in a recent California study. The gradient is clearly revealed only when comparisons are made between occupational groups in which the general mortality risk is similar. The apparently greater risk of coronary mortality in sedentary workers compared to heavy workers is of moderate degree, about 40 percent for occupations in the medium general mortality risk group. Factors that increase the general mortality risk and obscure the correlation with physical activity seem to account for as much coronary mortality as the limitation of physical activity.

In an analysis of survival and causes of death among almost 250 coronary patients comprising virtually all known cases in a small midwestern city who had survived their first clinically diagnosed myocardial infarction by at least 1 month, the survival rate after 3 years was 69 percent, after 5 years 55 percent, and after 10 years, 29 percent. The cause of death in the group was primarily cardiac in 82 percent of the deaths. The degree to which patients were able to resume preinfarction activity is apparently the best prognostic indicator.

Comparative studies of aortic and coronary atherosclerosis in India, Japan, Jamaica, and the United States indicate that after the first 20 years of life there is more pronounced alteration of the inner arterial wall in the United States than in the other population groups. It was also found that the incidence of coronary atherosclerosis and myocardial infarction was considerably greater in the U.S. sample. In the Japanese and Jamaican groups a greater severity of atherosclerosis was noted in the aorta than in the coronary arteries. This indicates that geographical variation exists with regard to the distribution of atherosclerotic lesions within the vascular system.

Diet studies

Research concerned with dietary aspects of cardiovascular disease has assumed increasing significance in recent years. Some of the recent findings of investigations supported by the Heart Institute in this field are given below.

Experimental studies indicate that the level of dietary magnesium may be involved in the development of atherosclerosis. Increased dietary magnesium has been shown to prevent development of lipid deposits on heart valves and in the aorta under various experimental conditions. This action does not appear to be related to the level of lipids in the blood. Studies are therefore underway to determine whether or not the effect of magnesium may be due to its action on components of the connective tissue which constitutes an important part of the arterial wall and can act as the site of abnormal fatty deposits.

Uracil, one of a family of naturally occurring compounds present in the daily diet of a large percentage of the U.S. population, is known to promote the elevation of serum cholesterol levels and cardiovascular lipid deposition, possibly via its effects on the thyroid. Recent animal experiments indicate that the simultaneous feeding of orotic acid, a precursor of uracil, markedly counteracts the action of uracil. The effect is particularly noticeable in female animals. It suggests further investigation to see if the lower incidence of atherosclerosis among women in the premenopause period is in some way associated with the metabolism of these compounds.

Recent diet studies with a low-fat food pattern and a vegetable-oil food pattern reveal that hyperlipemia in patients can exist in three forms, depending on the type of lipids involved, namely, neutral fats, cholesterol, or a mixture of these two types. In all patients studied with the mixed type of hyperlipemia or with high serum levels of neutral fats, the serum levels fell to nearly normal on the low-fat food patterns. Among patients with hypercholesteremia, although serum lipid levels were lower with either food pattern they returned to normal in only half of the patients. These findings indicate that knowledge of the patients' type of serum lipid abnormality is helpful in prescribing dietary treatment.

A long-term study of atherosclerosis in two monastic orders that differ significantly in their dietary habits, especially with regard to the consumption of fats, is yielding interesting results. One group, the vegetarian Trappists, consumes much less of its caloric intake from fat than the second group, the nonvegetarian Benedictines—26 percent compared to 45 percent. Considered as a group, it has been found that vegetarian monks at all ages have significantly lower levels of most serum lipids than do nonvegetarian monks. On an individual basis, however, there appear to be factors other than dietary fat intake and age that affect serum lipids.

The conduct of large-scale investigations over a span of time appears essential, if the preventive value of applying dietary changes suggested by past research findings is to be determined.

Grant support has been provided for the planning of comprehensive population studies on the relationship between dietary factors, particularly lipids, and the occurrence of atherosclerosis and coronary heart disease in representative samples of the population. Since these studies, when fully underway, may be extremely wide in scope, support has also been provided for one of several pilot studies which must be conducted to obtain needed preliminary information.

COMMUNITY PROGRAMS AND SERVICES

The heart disease control program, whose objective is to promote rapid and widespread use of research findings, furnishes technical assistance to the States to aid in achieving this objective.

Professional consultants and assigned medical officers and other personnel assist the States in field studies and demonstrations to test and improve detection techniques and methods of patient care. A year ago, 48 persons were assigned to provide such assistance. In many instances the lack of such personnel has prevented any activity in heart disease control.

The fiscal year 1961 appropriation has helped to meet the increased requests from States for technical personnel assistance and to raise this total from 48 to 69. This includes 47 medical officers and 22 nurses, nutritionists, physical therapists, medical social workers, and other professional health workers. In addition, five medical officers are in professional schools receiving specialized training which will increase their skills for assignments they will later receive in the States.

With the help of the added personnel, State and local health departments are offering many new or expanded programs in applied research and community services for heart patients.

An example of the potential in the newer kinds of community services to help physicians help people is the Georgia stroke rehabilitation project. This has dmonstrated that simple physical restoration techniques can be taught to health department personnel by a physical therapist. With these techniques, 80 percent of stroke patients meeting certain medical criteria, can regain independence in a number of daily activities.

Building on this experience, the control program has initiated stroke demonstration projects in many communities.

In Delaware County, a program medical officer assigned to the State is demonstrating that an effective home-care stroke program can be organized with medical elements already existing in the community.

Other programs—in Kentucky, Oregon, Colorado, and Ohio—are teaching proved methods of stroke patient care.

Validation of the fluorescent antibody technique for the rapid identification a group A beta hemolytic streptococci in human throat smears was announced on October 29, 1959.

Since that time, the control program has sponsored training in this technique for health department laboratory technicians in all States and territories, as well as four large cities. These technicians will in turn train personnel in private agencies and hospitals in their own areas. In addition, the control program has contracted with participating agencies for validating data and other information.

Use of this technique, coupled with antibiotic prophylaxis, can prevent first attacks of rheumatic fever and glomerulonephritis, and thus reduce the toll of rheumatic heart disease.

Commercial firms have begun production of a reliable specific fluorescent antibody or reagent, which will permit a more rapid and widespread use of the technique.

Technical and material assistance to States for in-State training courses will be a major undertaking of the control program during the coming year.

A long-range community program is being initiated in Bluefield, W. Va., with the cooperation of public and private organizations, to determine whether or not early drug treatment of mild hypertension decreases illness and mortality from cardiovascular-renal disease. This study will establish a pattern for other community studies in hypertension and cardiovascular diseases.

Tape recordings and readings of 33,092 children's heart sounds in Chicago have been completed. Although the analysis of results is still in progress, tape recordings of heart sounds, using specially developed equipment, appear to be a promising method of screening children for cardiac abnormalities.

A periodic clinical and laboratory evaluation of newborns through the fifth year of life is being planned in Pennsylvania to find a way to determine how early it is possible to detect congenital heart defects. At present the percentage of defects that become evident between the second and fifth year is not known.

There is a critical need for the standardization of laboratory procedures and tests in heart disease control studies. To answer this need, the control program, in cooperation with the Communicable Disease Center in Atlanta, has established a laboratory unit in Atlanta to serve as a "bureau of standards" for certain aspects of investigations in epidemiology. It will also provide fluorescent antibody services and work toward standardization of cholesterol, prothrombin, electrophoresis, and other laboratory tests relating to heart disease.

SUMMARY OF APPROPRIATIONS REQUEST

The amended appropriation request for 1962 is $97,093,000 as compared with the adjusted appropriation of $86,196,000 for 1961. This allowance for 1962 will provide for:

Research projects.—To provide for additional grants in support of new research in arteriosclerosis, cerebrovascular disease, hypertension, congenital heart disease, rheumatic fever and rheumatic heart disease, heart failure, coagulation defects, cardiopulmonary diseases, and other diseases of the blood and blood vessels, and for support of additional clinical cardiovascular research centers.

Direct research.—For relocation of part of the Laboratory of Chemistry of Natural Products into space presently used for offices, for development and initiation of further studies in the geographic pathology of heart diseases, for support of expanded biometric and epidemiologic research, and for studies on human exercise and fatigue.

Review and approval of grants.—An increase will provide for activities of the Institute staff and the National Advisory Heart Council necessary to the grants program.

Professional and technical assistance.—An increase will provide for expansion of control programs in hypertension and congestive heart failure and for increased activities on cerebral vascular disease and strokes.

Administration.—The increase will serve to strengthen program planning in the office of the Institute Director.

This request for 1962 is distributed among program activities as follows:

Grants:	
Research	$66, 187, 000
Fellowships	3, 100, 000
Training	9, 604, 000
State control programs	3, 500, 000
Subtotal, grants	82, 391, 000
Direct operations:	
Research	9, 900, 000
Review and approval of grants	1, 489, 000
Training activities	186, 000
Professional and technical assistance	2, 800, 000
Administration	307, 000
Subtotal, direct operations	14, 682, 000
Total 1962 appropriations request	97, 073, 000

Mr. FOGARTY. Go ahead.

Dr. WATT. There has been substantial progress made during this past year and I would like to tell you a few of the developments which, to me, are particularly exciting.

ELECTRIC PACEMAKER

Possibly you have heard about one of the items which I brought down to show the members of the committee. This is a small electric pacemaker, which is designed to make hearts "behave" or stay in normal rhythm; I suppose that would be the best way to put it. You can see it is about the size of a pack of cards.

This device is designed to take care of a condition which is a complication sometimes of elaborate heart surgery and, what is more important, occurs in older people as a result of arteoriosclerosis. This condition is one of the complications of a heart attack.

As you recall, the heart itself is really four pumps that work together by an electrical circuit within the heart. Sometimes there is damage to the nerves which carry the electrical pulse to the ventricles, which push the blood in the body and into the lungs. They have a protective device in that they have an independent rhythm of their own, but it is very slow—frequently too slow to keep the patient working effectively—and not enough blood is pumped out. In the course of repairing surgical defects in the heart, occasionally a suture will cause a sort of "short circuit" and this will cause heart rhythm troubles. The surgeons in the course of this began to use an artificial pacemaker which was a very elaborate piece of machinery kept in the operating room and which they could use only so long as the patient was very close to it.

Beginning a number of years ago in a number of places, actually through grant support, the development of a miniaturized pacemaker was started.

Work has been done on this by Dr. Lillehei out in Minnesota with Institute support, and in the Veterans' Administration hospital in Buffalo. The latter is not supported by the Heart Institute, but in Boston and at the Beth Israel Hospital work has also been done on this through some grants. We have now progressed to the point where there is on the market a pacemaker of this type as well as another one.

The one I have here is one we have in reserve at the clinical center where we have a patient there wearing one of these, and he is able now to walk around the building quite comfortably as a result of having this available to him. This one is worn outside of the body and the rate can be changed by turning this little dial here [indicating]. You can slow down this flashing light or speed it up.

There is another one which is even more interesting, but before I go on to that, this one is worn with a connecting wire. It is not impervious to fluids. You cannot get it wet, so when you take a shower you have to put it in a plastic bag and hang it on the wall. This is the wire [indicating] that goes through the skin and into the heart itself. The metal hook is inserted in the heart muscle and that carries the current to the heart. Each time the light flashes, it gives a little electrical stimulus and causes the heart to beat.

The patient can slow it down at night. When he is walking or taking exercise or when he is on the job, as some are now, he can turn the rate up a little bit if there is an extra demand.

The newest type and one which is just coming into use now is embedded in a plastic that is impervious to body fluids. The surgeon makes a little pouch down in the ribs and can actually insert the tiny pacemaker under the skin. There is no external wire. The wires are all hidden, and the batteries have a shelf life of about 10 years. It is believed that they have a life in use of about 5 years.

Mr. Fogarty. How do you control it?

Dr. Watt. That one has to have a set rate. It does not have an outside control so the surgeon must adapt it to the patient's basic needs. It does not have the ability to speed up for exercise but it can be set at a rate that will remain quite useful for ordinary activities.

Mr. Fogarty. What will this do? Give me an example of how the patient is affected.

Dr. Watt. What happens is that the ventricular rate, the rate of the major pumps of the heart, is quite slow and when there is a block between the point where the electrical stimuli originate in the heart and the ventricles of the heart, the ventricles go to their intrinsic rate which is less than half that of the heart with normal conduction. The normal pulse is somewhere between 70 and 90, and when the block occurs it will drop down to the ventricular rate, which can be as low as 25 or 30 beats per minute. This is not enough.

Mr. Fogarty. How does that affect the patient?

Dr. Watt. Usually they do not get enough blood for normal activity. They have to lie at rest and cannot carry out their normal activities simply because of a lack of oxygen to the working parts of the body. Because of this lack of oxygen, they are incapacitated. They cannot carry out their regular work.

TYPE OF PATIENT BENEFITED

Mr. Denton. Do these benefit arteriosclerotics? Is that the kind of people they benefit?

Dr. Watt. Arteriosclerosis can cut off the blood supply to the heart in places. If the coronary blood vessels are blocked and if it occurs at a place where it damages this electrical mechanism, then it would be a result of the arteriosclerosis. There are other causes of heart block, such as the one I mentioned, a complication of surgery. This pacemaker lets us introduce a control which will artificially keep the heart going at a rate that is consistent with the activities of that individual.

This one has a safety device on it, as you can see. You cannot cut that light off unless you positively push this button down with force. It cannot be accidently turned off.

I asked how a patient would know when the battery was running down. I thought it might quit on them or something of that sort. I do not fully understand the electronics of this, but as the batteries get weaker, they begin to fire at a faster rate so that the heart is actually speeded up as the batteries get older. The patient can tell by his pulse rate that the batteries are running down and then come in and change the batteries. The batteries are small ones like this [indicating] and can be used in this pacemaker.

It is a very interesting development of many, many lines of research coming together, because part of this is the development that has gone into the electronics business. The development of transistors is one of the things that has made it possible to miniaturize the pacemaker. The ability to imbed it in the body is a result of developing plastics which are impervious to body fluids. This piece of work has taken many years and is making it possible for these patients to go about a perfectly normal life, not much different from the people who wear a hearing aid.

This device is about the same size, and has about the same degree of complexity in its use.

In thinking about other lines of research, I would like to mention some of the types of activities now.

CONTROL OF THE BLOOD'S CHOLESTEROL LEVEL

MER-29

Another area where there has been considerable development during the past year or more, and which is of particular interest to this committee, is in the evaluation of drugs, finding out more about how they can be used effectively in the prevention of illness as well as in its treatment. During this past year, the Heart Council has given particular attention to this and, under the chairmanship of Dr. Robert Wilkins, has a group working very hard on the planning of a study which would evaluate drugs used in lowering cholesterol. As I mentioned last year, there are now available a number of drugs which do affect cholesterol. We have learned a lot about how this happens in the body, but there is a problem of very real concern.

We now know, for example, of a drug called Mer-29 which blocks cholesterol synthesis in the body, and it does so at a point which the chemists speak of as demosterol, which is one point before the body makes cholesterol itself. The use of this drug leads to the accumulation of demosterol in the body. It is not a steroid that we know very much about. Normally it goes very quickly from that step to cholesterol, so while the drug clearly can cut down on the amount of cholesterol that will be produced by the body and accumulated, it also leads to the accumulation of demosterol. So far in its use no evidence of toxicity has developed, but this may well be because we do not know what the toxic effects of demosterol may be.

These effects may be much the same as cholesterol for all we know. Therefore, it is quite important we not only study the basic chemistry of this material but also find out what happens in the individuals who have been treated with this particular drug. There are many people who have been treated with it now, but there has been no really systematic way developed for following up on them. It has been done in many places on a small scale, and I think it is most important we now have ways and means to put together quickly and systematically the research of these individuals and some standard way of comparing their results so we can determine just how much benefit this change in the body chemistry will be to the individuals. It has been almost axiomatic that lowering cholesterol will be beneficial to patients. This is based on the fact that in many diseases where cholesterol is quite high that there has been a high amount of arteriosclerosis or hardening of the arteries.

What has not been demonstrated is the degree that lowering cholesterol and keeping it down, by means such as a drug where you interfere with this metabolism, will actually lead to longstanding benefits.

CHOLESTEROL-FREE DIETS

Mr. FOGARTY. I was asked last year by a Member of Congress if you had a cholesterol-free diet.

Dr. WATT. There are a number of diets that have been designed, both low in cholesterol and free of cholesterol. The problem that any individual faces is, if his system is capable of making quite a lot of cholesterol, a cholesterol-free diet will sometimes have very little effect on the amount that will build up. It will lower it for a while only.

Mr. FOGARTY. Should he go to his own doctor?

Dr. WATT. Yes; I think the main point there is to let the individual physician study it and find out just what will happen when he is put on these different diets.

Incidentally, at the present time we have also underway another collaborative study under the direction of Dr. Page in Cleveland where they are hoping to find out what will happen in a large population group when dietary means are used for lowering cholesterol. We can lower cholesterol by dietary means in highly selected cases, and it is believed that this can be achieved on a normal home diet by proper consideration of food content itself.

Mr. DENTON. In that connection, somebody told me that cholesterol was very bad for some people and did not hurt other people at all. It affected different people in different ways.

RESEARCH ON VARIATIONS IN CHOLESTEROL ACCUMULATION

Dr. WATT. Certainly we do not know enough about how cholesterol is handled by different individuals. There is a tremendous variation, Mr. Denton, between the ability of individuals to handle it. One of the more interesting developments in this past year in Bethesda—Dr. Shannon referred to it in his opening statement—is the study that has been going on in the Heart Institute which shows that not only does the way we handle cholesterol vary from individual to individual, but within the same individual.

They have shown that cholesterol accumulates much more rapidly in the upper part of the big artery in the chest, the aorta, than it does in the lower part down in the abdomen, and a high cholesterol diet that was given to a dog showed it will accumulate cholesterol much more rapidly in the upper part of the aorta than in the lower part. Keeping this up over a period of time, you wil find that this reverses itself because the rate at which the aorta disposes of the cholesterol is greater in the upper part than it is in the lower. While it is collected faster, it is also gotten rid of faster in the upper part of the aorta.

This question of what damage cholesterol causes is not just a matter of how much is floating around in the blood, but also what happens to it when it is deposited in different parts of the body. This is a very complex problem and the experiments that are going on are adding pertinent pieces to this formula. I am quite sure that with patience, and with the persistence that these men are working on it, we will have a much more simple explanation than we have at the moment. It is quite clear that it is not just a matter of how much to take in, or even how much is in your blood, but a question of what happens to it when it gets to those parts of the body where it does not normally accumulate and where it causes damage. We believe it can cause damage if it is there in excess amounts.

These two types of studies are complementary to each other.

CONTROLLING ACCUMULATION

Dr. Wilkins is planning to study what happens when drugs are a method of modifying cholesterol and Dr. Page is focusing on what happens when diet itself is used as a means of modifying cholesterol. They are working very closely together and our staff reports are going to be available to each group, so that as they plan it, to whatever degree it is possible they can use common controls and common systems of communication which will make it a lot simpler and a lot less expensive than it otherwise would be.

If it is carried out, it is actually going to be a very time-consuming and very expensive program. It is one that will take a tremendous amount of organization before it can actually be gotten underway, and I do not know how far the study committee feels it can be pushed, but the last report I had is that they had a meeting just this past week in Cleveland, and they had two major problems that they were concerning themselves with at this time.

One is how to maintain observation of a large number of people who must be scattered all over the country to get any clear picture. How can that observation be maintained consistently with people moving around as much as they do?

DEVELOPMENT OF STANDARDS

The other problem was one that was faced back when they had a collaborative study some years ago on the ultracentrifuge work, the need for development of standard methods for various groups. We still have a major problem of standardized methods, or methods that provide for direct comparison between laboratories.

Dr. Felix in his testimony yesterday mentioned some of the difficulties that were encountered in this respect and we have it here, too. We have, during this past year, made some significant progress in this respect in collaboration with the Communicable Diseases Center in Atlanta. We have been working through our technical assistance program to develop standards whereby any laboratory can compare its cholesterol determinations with the standard in Atlanta and with each other. I am sure this is going to be a major assist, not only to the laboratories working on this collaborative study—we have used our Framingham Laboratory and a number of others doing these field studies—but we will make this type of standard available to other laboratories who wish to develop a means of comparing their results.

I think it would be fair to say, however, that the need for standards is not just in that field. I remember Dr. Masland was speaking about the need for this in defibrinolytic agents, the ones that dissolve clots. Here is a very difficult field partly because of the lack of a standardized product, a product not only consistent from day to day, but between several different kinds of products. This whole area of biological standards is a terrifically difficult one and particularly so when it is used in this laboratory work.

EPIDEMIOLOGY

THE BRITISH ISLES

Another area I would like to speak of briefly is in the field of geographic pathology or epidemiology. Some 3 years ago, in discussions that the National Heart Institute had with several people, it was brought out that there was a striking difference in mortality between the United States and the United Kingdom, as reported in the official Registry of Births and Deaths. There is a great deal more disease of the pulmonary-heart complex, the cardiopulmonary diseases, cardiobronchitis, in the British Isles than in this country.

We suspected it might be a question of clinical diagnoses being different and habits of diagnosis being somewhat different, but it also seemed to be much too great to be just a matter of impression. So there was organized a small group to take a look-see at that phase of it as well as look into the statistics themselves. This was under the direction of Dr. Reed of the London School of Tropical Medicine and Dr. Harold Dorn, who at that time was working in Dr. Shannon's office but who is now in charge of biometrics research of the National Heart Institute. These two men have worked with clinicians and they have gone over patients in the British Isles and they are planning a further study of that in this country this year. The impression so far has been confirmed that this is not just a matter of clinical diagnosis, and that there is quite a difference in the disease itself.

Further exploration of the statistics indicate that not only is this a fact that there is a great difference, but these cardiopulmonary diseases are on the increase in this country. As reported here, they seem to be definitely showing an increasing trend and why this is so we do not know. One of the reasons we feel this should be pursued quite intensively now is that if it is a definite increase, now is a very important time to begin such a study because if you can detect it in an early phase, it is a lot easier to understand some of these complex relationships than if you wait until many years after the event.

There are now going on studies to help find out about this difference. I was impressed by this and I had a note here to comment on this, Mr. Fogarty, which fits in with Dr. Shannon's discussion yesterday on Puerto Rico.

PUERTO RICO

I was recently there and went over at some length some of the reports they presented at the time of the White House Conference on Aging. It is extremely interesting to look at the mortality in that island. When I lived there 20 years ago the expectation of life at birth was in the lower forties, if I recall correctly. Now it is quite comparable to the mainland of the United States. This means, with the rapid shift that you actually have in virtually all age groups, a lower mortality at the present time in Puerto Rico than in the United States.

There has been a steady fall in mortality in all age groups. Dr. Arbono, Puerto Rico's secretary of health, is watching this very carefully because he says it is perfectly obvious that this will have to begin to rise again sometime as the population grows older. He is very much interested in knowing where will the effect of this saving of lives in younger years begin to show up in diseases of later years. I think it is one of the most important opportunities we have for an epidemiological study at the present time, to carefully work with them in following this development on the mortality figures in the island of Puerto Rico. Interestingly enough, too, if you had asked me last year whether they had problems in the field of aging, I would have predicted that there would be another 40 or 50 years before they approached the same type of population distribution as in the United States, because they had just recently reduced their mortality.

Actually, this would have been based without regard to the fact of immigration and migration, and they are rapidly assuming a population distribution that is very much like the mainland of the United States because many of the young people are coming to the United States to work, and those who have lived here many years are going back home as they retire. Consequently, you are getting a very rapid movement into the older age groups.

In addition to that, there is a very marked change in their society taking place, whereas when I lived there it was virtually all rural. Now within the last 2 years their economy has shifted so that income for the last 2 years has been more from industrial sources than from agricultural sources. You are having a very marked change in the family life, the way they are living, and their housing, and it looks to me like they may be facing the problems that have grown up gradually in some of the older parts of this country on an acute basis.

If this is so, it again may be one of the more important places to learn how to handle some of these problems.

We spent quite a lot of time talking to Dr. Arbono and members of the Puerto Rican Planning Commission while I was there and I believe there will be a number of things we can do that will be most useful. We have agreed to continue to work out plans for studying this phenomena which I am sure will be most helpful to us.

DISSEMINATION OF NEW MEDICAL INFORMATION

If I may, I would like to emphasize just one more point and that is, that as this knowledge is accumulated, I think we can be pleased with the progress we have made, and the use of it, but also a little disappointed that it has not been used more rapidly. I think we are making plans which, in the course of the next year or so, will result in speeding this process from the laboratory to the patient and to the person in the community very definitely.

This is particularly true in working with the State and local health departments, working with members of various community hospitals, to find ways and means of systematically bringing to the attention of the people in the community the products of research. I hope that I can see it real soon.

I was talking to a doctor recently who was telling me he was running courses for patients in his community. He was bringing them into the hospital on a systematic basis, they were drawn from different parts of the community, and he was trying to teach them how to be good patients.

He had some very simple and interesting lectures on how the circulation developed, how it started, and what it is in the human being, with the idea that when they come into the hospital with any form of illness, heart disease or whatnot, they would understand why the doctor wanted them to do certain things and thus would be much more cooperative and much more likely to benefit from the hospitalization. He feels this will be a significant factor in actually cutting down on hospital time and cutting down on the problems a physician always has to try to persuade the patient to be cooperative and do the things he thinks he should do.

A lot of this is going on around the country, and I believe we can, by better means of communication, speed up this process tremendously. We are working quite hard at that, and I hope the results will be apparent not only to those of us who are working in it but also to the community.

These are the main points I would like to emphasize, Mr. Chairman. If there are other questions you would like to raise about this, I would be very glad to answer them. The budget before you today I am sure will give us a chance effectively and aggressively to push the programs which I have not had time to cover in the statement.

ADEQUACY OF THE 1962 NIH BUDGETS

Mr. FOGARTY. Dr. Shannon, have these Institute Directors all been told or been given orders to say this budget would allow a lot of progress?

Dr. SHANNON. No, sir.

Mr. FOGARTY. Everyone seems to go out of the way to make sure they get that statement in. I wondered whether they had orders from you or from the Surgeon General or the Secretary.

Dr. SHANNON. No, sir. They have been told to recognize that this budget does represent increases in certain areas of their program, but beyond that they have received no specific instructions as to how they should interpret them.

Mr. FOGARTY. That is the pattern which has been followed the last couple of days. The statement has been made repeatedly that the budget would allow significant progress. I just disagree with that kind of statement. I think in some areas you are going backward, not ahead. I thought maybe they had some orders to make this statement to lead people to believe that real progress will be made with this kind of budget, which is about $100 million short.

Dr. Shannon. I think they would say, if questioned generally, that the budget does permit the continuation of programs initiated during the past year and is sufficiently large in the current year to undertake certain programs and extend certain programs which they consider to be highly essential. I do not believe they would agree in general, quite apart from any discussions I may have had or Dr. Terry may have had with them——

Mr. Fogarty. I do not see how we can put much credence in it when they asked you for a lot more money when they formulated their budget. It does not make sense to me to ask for $25 or $30 or $40 million more and then be allowed only $3 or $4 million, and then to say this is a good budget.

Dr. Shannon. I do not believe they have said that in those precise words.

Mr. Fogarty. Not in those precise words. Those are my words. That is the way I understood it. Let me put it that way. I am not blaming them. I am not blaming you, either, if you received those orders.

Dr. Shannon. No, sir.

Mr. Fogarty. I have been around here a little while, and I know how these orders come out. I understand your position. I am trying to help you. I am concerned about these individual programs and how much is needed. I have been convinced for a long time that if we spent a little more money in some of these areas we could save money in the long run. Is that not a fair statement?

Dr. Shannon. I believe it is, sir; yes, sir.

THE 1962 BUDGET

Mr. Fogarty. Dr. Watt, the appropriation for 1961, less comparative transfers, is $86,196,000, and the Eisenhower budget is $91,357,000, an increase of $5,161,000. The budget amendment is a further increase of $5,716,000, or a total increase of $10,877,000 over the 1961 appropriation. But there is a nonrecurring item of $2,366,000 for adjustment of training grants. So the real increases are about $7.5 million in the Eisenhower budget and $13.2 million in the revised budget. Does that sound right to you?

Dr. Watt. Yes, sir.

Mr. Fogarty. As usual, will you put in the record the history of your 1962 request and the history of the budget amendment?

Dr. Watt. Yes, sir.

(The information requested follows:)

Development of 1962 budget estimates for National Heart Institute

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$84, 818	+$928	$85, 746	−$14, 331	$71, 415	−$9, 995	$61, 420	$74, 358	$8, 171	$66, 187
Fellowships	3, 400	0	3, 400	0	3, 400	−300	3, 100	3, 400	300	3, 100
Training	15, 594	−5, 990	9, 604	0	9, 604	0	9, 604	9, 604	0	9, 604
State control programs	5, 000	−1, 500	3, 500	0	3, 500	0	3, 500	3, 500	0	3, 500
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	108, 812	−6, 562	102, 250	−14, 331	87, 919	−10, 295	77, 624	90, 862	8, 471	82, 391
Direct operations:										
Research	9, 954	−115	9, 839	−127	9, 712	−390	9, 322	9, 900	0	9, 900
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	1, 527	−205	1, 322	+21	1, 343	−29	1, 314	1, 668	179	1, 489
Training activities	227	−41	186	0	186	0	186	186	0	186
Professional and technical assistance	3, 337	−180	3, 157	−357	2, 800	−178	2, 622	2, 800	0	2, 800
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	354	−59	295	0	295	−6	289	307	0	307
Total direct operations	15, 399	−600	14, 799	−463	14, 336	−603	13, 733	14, 861	179	14, 682
Total obligations	124, 211	−7, 162	117, 049	−14, 794	102, 255	−10, 898	91, 357	105, 723	8, 650	97, 073

Mr. FOGARTY. What did you ask for?

Dr. WATT. Approximately $124 million.

Mr. SEGGEL. $124,211,000.

Mr. FOGARTY. What did you get?

Mr. SEGGEL. $97,073,000.

Mr. FOGARTY. This left you short $27 million. Do you still think you could use that $27 million if the committee decided to give it to you?

Dr. WATT. Yes, sir.

Mr. FOGARTY. Do you think you could use another $50 million if they decided to give it to you?

Dr. WATT. That is a question I would want to look at and think about, Mr. Fogarty, before I answered directly, sir, if I may. I do not have any plan——

Mr. FOGARTY. I will put it another way. You can use the $27 million that you asked for, efficiently and wisely?

Dr. WATT. Yes.

Mr. FOGARTY. You can supply for the record how you would use another $50 million.

Dr. WATT. Yes, sir.

(The information requested follows:)

NATIONAL HEART INSTITUTE

Tentative distribution of increased funds for 1962

[In thousands]

Activities	Original estimate to NIH	Use of additional $50.000	Total
Grants:			
Research	$84, 818	$17, 553	$102, 371
Fellowships	3, 400	1, 700	5, 100
Training	15, 594	1, 406	17, 000
State control programs	5, 000	2, 000	7, 000
Total grants	108, 812	22, 659	131. 471
Direct operations:			
Research	9, 954	2, 046	12, 000
Review and approval of grants	1, 527	673	2, 200
Training activities	227	273	500
Professional and technical assistance	3, 337	12, 203	15, 540
Administration	354	146	500
Total direct operations	15, 399	15, 341	30, 740
Construction of gerontology building	0	12, 000	12, 000
Total estimate	124, 211	50, 000	174, 211

INCIDENCE OF DEATH DUE TO HEART DISEASE

Mr. FOGARTY. Is it still true that heart disease causes more deaths than all other diseases put together?

Dr. WATT. Yes, sir, that is true. It is something like 53 or 54 percent of the deaths in this country today.

Mr. FOGARTY. Over 900,000 people die every year because of some form of heart disease. Has that been fairly steady for some time now, that 900,000 per year figure?

Dr. WATT. Approximately that, Mr. Fogarty; yes, sir.

Mr. FOGARTY. With the increase in the population, does that mean the rate is going down some?

Dr. WATT. Actually, within the group of heart diseases there are some of these conditions that are going down and some that are going up. In the case of rheumatic heart disease, we can report very definitely a beneficial trend. It is going down. In the field of hypertension, there has been definitely a trend in that respect. However, as I reported a little earlier, there is clear indication of an upward trend in the field of the cardiopulmonary diseases, the ones where the heart is enlarged through lung trouble and this type of thing. We do not fully understand it, but we at least have recognized it early and I believe have studies underway which will be helpful in bringing out some of the factors here.

Mr. FOGARTY. That kind is going up?

Dr. WATT. Yes, sir.

Mr. FOGARTY. Perhaps you should redouble your efforts in that area.

Dr. WATT. That is an area in which I am convinced very profitable work can be done at the present time.

Mr. FOGARTY. But the 900,000 figure, or whatever the exact figure is——

Dr. WATT. Actually, Mr. Fogarty, in 1959 there were 898,000, so the number of 900,000 is very close.

Mr. FOGARTY. But our population has been growing every year, and this figure has been remaining about the same, has it not?

Dr. WATT. Approximately. These diseases are reported on the population increase which took place a good many years ago. The bulk of the heart diseases, other than the congenital ones, occur in later life. So the population growth which took place 40, 50, or 60 years ago is the population growth which leads to the change in incidence in the population here.

Actually, the total number of deaths has been gradually increasing year by year for a good many years now.

EFFECT OF INCREASE IN 1962 BUDGET

Mr. FOGARTY. Will you provide for the record how the original increase of \$7½ million would have been applied, and then what effect the further increase of \$5,700,000 would have on your 1962 program?

Dr. WATT. Yes, sir.

(The information requested follows:)

Statement on use of increases in 1962 original and revised estimates

	Increases in original estimate	Additional increases in revised estimate	Total increases in revised estimate
Grants: research	\$6,347,000	\$4,767,000	\$11,114,000
Direct operations:			
Research	814,000	578,000	1,392,000
Review and approval of grants	80,200	175,000	255,200
Professional and technical assistance	271,000	178,000	449,000
Administration	28,500	18,000	46,500
Total increases	7,540,700	5,716,000	13,256,700

BACKLOG OF APPROVED RESEARCH GRANTS

Mr. FOGARTY. What will be the total of approved but unfunded research grant applications at the end of 1961?

Dr. WATT. At the end of 1961, at the end of the last Council meeting, there was something over $3 million. I believe you have those figures.

Mr. SEGGEL. Mr. Fogarty, assuming institutional grants do not start in 1961, and approval by the Bureau of the Budget of our request to release unprogramed funds, the deficit would be $1,468,000 at the end of this year.

Mr. FOGARTY. What about 1962?

Mr. SEGGEL. $6,071,000, assuming institutional grants start in 1962.

Mr. FOGARTY. If they do not start?

Mr. SEGGEL. $3,506,000.

INCREASED PAY COSTS

Mr. FOGARTY. I notice an item for each Institute called "annualization of pay increases." In yours it amounts to $6,000. What is that?

Mr. KELLY. This is the 6-day annualization amount. It occurs because the pay increase was not in effect during the first 6 days of 1961.

Mr. FOGARTY. How much of the pay increases did you absorb in 1961?

Mr. SEGGEL. For just the Heart Institute? We absorbed about $3 million total. I do not know what the figure is for the Heart Institute.

Dr. SHANNON. We can break that down for you.

Mr. SEGGEL. We can supply that for the record.

Mr. KELLY. $421,000.

Mr. FOGARTY. Is that all of it?

Mr. KELLY. That is all of it.

Mr. FOGARTY. You are not getting an increase for that in 1962, are you?

Mr. KELLY. Only to the extent of the reinstatement of the 3 percent absorption, the item we have already mentioned in previous hearings.

INCREASED COSTS

Mr. FOGARTY. What increased costs have occurred in the last year?

Mr. KELLY. I do not have an estimate. You mean with respect to the grant program?

Mr. FOGARTY. Yes.

Mr. KELLY. I do not have that.

Mr. FOGARTY. For the Heart Institute. Can you supply that for the record?

Mr. KELLY. Yes.

Mr. FOGARTY. Make an estimate. It would have to be an estimate.

(The information requested follows:)

NATIONAL HEART INSTITUTE

The research and training grant programs would require an additional $2 million in order to maintain in 1962 the 1961 program level. This estimate is based on the increase of 3.7 points in the index of prices on all Federal purchases of goods and services reported in the Economic Report of the President, January 1961.

CATEGORICAL CLINICAL RESEARCH CENTERS

Mr. FOGARTY. Doctor, I think Mr. Laird will want to ask you some questions about these centers, but you might give us a short résumé of the program for the categorical clinical research centers.

Dr. WATT. Mr. Fogarty, I will have to be a little bit qualified in my statement, since the National Advisory Heart Council has not yet passed on any of the clinical center grants. We have a special meeting of the Council to be held on April 17 and 18, at which all of the applications which have been received this year will be reviewed at one time. We are still in the process of making project site visits to the applicant institutions.

Mr. FOGARTY. What is the number of applications you have?

Dr. WATT. We have had 49 applications which will be reviewed at that time.

Mr. FOGARTY. And the dollar amount?

Dr. WATT. $22 million is the total requested.

PRIMATE COLONIES

Mr. FOGARTY. What about your work on the primate colonies?

Dr. WATT. This also will be reviewed and final recommendations made at the special meeting of the Council. This year we have in hand 23 applications for primate centers. The total requested is some $26 million. I have requested the Primate Committee, which is chaired by Dr. Karl F. Meyer, to do a little more than just review the applications. Now that they have seen all of the areas of this country which are interested in developing these facilities, I have asked that they make recommendations as to where we can best achieve the scientific merit aspects of the program as well as a geographic distribution which will permit easy utilization of these regional centers. This will also be brought to the Council at its meeting.

It seems as if we have very good opportunities for achieving this balance of geographic distribution and scientific interest. One grant was awarded last year, as you recall it, at the University of Oregon. The other places that are being considered are scattered over the country; the Northeast, Midwest, Southwest, and Southeast all having places which are quite interested in developing these centers, and some very good plans have been submitted.

These project site visits have all been completed.

ARTERIOSCLEROSIS

SATURATED AND UNSATURATED FATS

Mr. FOGARTY. In the area of arteriosclerosis, what about the problem of saturated versus unsaturated fats? Have you reached any conclusion?

Dr. WATT. Yes, sir, they have reached a number of conclusions. One of the difficulties in this field is really the rather large number of clues which have turned up as to what may influence the progression of arteriosclerosis. I think we can say that within the last year or two there has been enough crystallization of thinking and ideas that we can systematically approach this now in two quite different ways.

One is the continued support of those individual researchers who are digging into the way fats are handled by the body, the whole metabolism of fats and the different aspects of it. This we are continuing to support as we have in the past.

The important addition in the way of looking at it is that now many people who have been doing this feel that experiments can now be designed which will test in man the effect of fats on the occurrence of heart disease. This is a beginning to get at prevention rather than just treatment, of determining whether or not effective modification of the way we handle our foods in our home, if you will, can actually do something about prevention of disease.

Mr. FOGARTY. Will these people all be volunteers?

Dr. WATT. One of the problems which is being considered right now, Mr. Fogarty, is what type of population would be best susceptible to it. One of the questions raised was whether a population such as a military population might be useful. This has been considered and rejected as being not very suitable for this type of study, because the men in the military are a highly selected group and are kept under very close surveillance. Such a study would not tell us very much about what goes on in the normal population. The group that is working on this is planning to draw the samples from different parts of the country and it would be a simplified approach. Each individual spot would be somewhat analogous to our Framingham studies, but would be much more sharply focused on the particular question of whether modification of the foods in the diet can effectively prevent the occurrence of coronary occlusion. In addition, most of the researchers feel they should include observations as to the effect of this diet modification on cholesterol and some of the other fatty materials in the blood. This is one of the biggest points of discussion, since many feel that there are different indexes which could be used and at this point there is no general agreement on what would be the most effective one to use. I think they are making progress, though, in finding agreement on that point and, when they do, I think we will be ready to go.

Mr. FOGARTY. It will be a long, long time if you operate on this kind of budget. That is not your fault.

DIAGNOSIS BEFORE AN ATTACK

Do you have any method of diagnosis before an attack?

Dr. WATT. To answer that precisely, I would have to say no, sir. I think there are ways and means of determining high risk groups of people, and there are a number of factors that tend to let you identify people who have a higher than normal risk.

Mr. FOGARTY. Is that through statistics that you reach that conclusion?

Dr. WATT. Through statistics and careful histories of individuals and studies of families. One of the more interesting approaches is in a small town in Michigan with a group of families which has had high cholesterol. A very serious field study is being put on there under the direction of Dr. Francis of the University of Michigan, where they are really trying to find the susceptibles. I think, if you can simplify a complex problem, the objective and goal they are shooting for is to identify the susceptibles in the community and to do so with a degree of precision which is better than the simple statistical approach, which is about all we have had up until now.

FRAMINGHAM STUDY

Mr. Fogarty. How long has the project at Framingham been going on? Eight or ten years?

Dr. Watt. Ten or twelve years now, Mr. Fogarty.

Mr. Fogarty. Have you any results to report?

Dr. Watt. Yes, sir, as a result of the 10th year summary.

Mr. Fogarty. Tell us what it is, and what some of the results are.

Dr. Watt. All right, sir.

HISTORY

In Framingham, about the time that the Heart Institute was created by the Congress, there was a plan to study a community to determine what happens to the people in that community with respect to the occurrence of various cardiovascular circulatory diseases. The town of Framingham was selected because of its location, the fact that they had participated earlier in a similar study with respect to tuberculosis, and because it was a place where there was access to a medical community nearby, so the men working there would have the opportunity of discussing their problems with men in the schools in the immediate general area. A sample of that community was selected to be representative of the community, and a systematic followup put on. We do not treat the patients, we do not enter into the question of care, but merely follow them carefully over a period of time with biennial physical examinations, with a number of tests which are part of a standard procedure. Then from year to year we have added new means of observing the patients.

This study has given us data which are not available anywhere else in the world about the natural history of various heart diseases. It also has been the standard, if you will, against which a number of other studies have been developed and will give us by comparison and by pooling of results some quite definite answers that are difficult to get in a small population group.

One of the problems with Framingham is that it was set up for a long-term study simply because there were not enough people able to be followed to have enough of these diseases develop to get an answer quickly. The problems of how to follow up people are not inconsiderable. With, however, the experience gained there, there are a number of other studies which are going on in this country which will permit pooling of results over a period of time, and there has been active collaboration between Dr. Thomas Dawber, who is in charge of the Framingham study, and some of the men working in other areas following an analogous plan.

RESULTS AND PROSPECTS FOR FUTURE

Our own observations there have shown that people who have a higher-than-average cholesterol level have a higher-than-average risk of coronary heart disease, some three to four times. Similar observations are true with people who have a higher-than-average blood pressure. These two things together seem to have an additive effect to each other. In other words, taking both variables, the increase goes up sharply.

We have been looking at other variables as to what factors may be related—the question of excess weight and smoking. Now we are beginning to look at such questions as vital capacity, the degree of anemia, whether or not the blood has a high red cell count or a low one. This type of thing is being looked at to see what relationships may appear.

One of the interesting points that came out from Puerto Rico was the fact that in areas where the nutrition had been low, it was demonstrated many years ago that the heart developed quite a lot of collateral circulation when there was anemia. You have the opportunity in a place like Puerto Rico to study what effect some of these tropical anemias have on the circulation of the heart. Quite possibly this anemia might be protective in an older person if there is good collateral circulation. This might be a protective factor. It is an interesting suggestion but we do not have any real proof. But this observation of markedly greater blood vessels to the heart itself in people who have had a longstanding anemia was made down there many years ago. They are planning in their school rather aggressively to develop studies which would show this interrelationship. For some of these populations like Puerto Rico and possibly some of the other countries where coronary heart disease is of low occurrence, it might be an explanation of why this relative difference exists. We do not know that, but we are looking into it.

We have also instituted in Framingham an attempt to measure the question of stress and what effect this may have on some of the body functions. We have begun to have an analysis made, by collaboration with the Worcester Foundation near there, of the hormones that are put out in the urine. This demonstrates again the interrelationship of these fields. I had the privilege of listening to Dr. Felix. as he commented on the collaboration we have had. This is another way of looking at the same problem of how these hormones control not only the problems related to heart disease, but also are very important in some of the mental illnesses that he has studied.

As we develop profiles of individuals on their hormonal excretion, I think we will have a much better understanding of how these diseases do fit together.

Mr. Fogarty. Is there anything other than diet or loss of weight that will lower your cholesterol?

Dr. Watt. There are drugs which will modify the cholesterol in the blood at the present time. This is being tried on a clinical basis, and quite a lot of work is being done at the present time. There are those who believe that it is possible by studies of exercise to show ways and means of having the body burn these fats more effectively. There are about five things that can affect it. It is a matter of how they balance out within an individual and how his own mode of life lets him effectively balance these factors. If we could once get one of them as a constant, we would be a lot better off, but all of them vary from individual to individual, and it makes for a very complex equation to try to get an answer.

STROKES

Mr. Fogarty. What progress are you making on strokes, Doctor? We have heard of some progress from Dr. Masland.

Dr. Watt. I would like to begin the answer by telling you we have recently worked out with the National Institute of Neurological Diseases and Blindness a joint council committee for pushing those things which can be done best jointly, thus having a study which would show the interrelationship between the programs of the two Institutes—this has been set up, and we will be working together from now on. In addition to that, we have two studies on a collaborative basis, which are aimed at the prevention of strokes by means for early diagnosis.

Dr. Michael DeBakey and a number of others have been working on the blocking of the arteries of the neck. These can be repaired surgically now. The problem to which they have addressed themselves is how to diagnose these cases early so they can repair them before the stroke actually takes place. This is not too technically difficult an operation, but you do not want to subject any patient to an operation unnecessarily. At the same time, you would like not to have to wait until he is critically ill before you remove the artery block. So it is a matter of studying people on a wide basis by neurologists, surgeons, and medical men, all three, to determine when is the effective time for removing one of these artery blocks before it actually causes brain damage.

This has been going on now for about a year and a half, and it is my understanding that they already are getting results which are useful in the cooperative clinics and that they will in turn have some results which they can make much more widely known in the near future.

The other side of this is in the home care of patients who have had strokes. The State of Georgia has done a terrific job of bringing early rehabilitation into the home. They approached it in three steps. You know of the clinics started by the Heart Association there in collaboration with the State health department (which used some of our State grant funds to help these clinics get started). These Heart Association clinics now cover the State. First, through those clinics, they got the physician acquainted with what could be done by early manipulation of the paralyzed limb, so there is no damage. They then organized a program of bringing nurses from the State health department to Atlanta to learn this manipulation at the Grady Hospital which is connected with one of the clinics. The following year these nurses were sent to the individual communities, to teach the family of the patient. So, when a doctor has a stroke patient, a public health nurse goes to the home and shows the family how to carry out these exercises which are so important if the patient is not to suffer far more damage than necessary.

This now is on a statewide basis, and we hope during the coming year to have a series of clinics or teaching sessions which will permit this State plan to be taught in other areas that want to try it. There are other States which are starting on it. Pennsylvania has quite a good program in this respect.

From the results I have heard from Gordon Barrow, who is in charge of the program in Atlanta, I think it is an exciting development and one which is doing a tremendous amount of good to patients in that area. The physicians can use these nurses, and it is very quickly possible for them to demonstate what can be done in the home. The families usually are quite scared of a paralyzed limb.

They worry about it. Is it going to fall off or will they damage it? They need somebody to show them just how much pressure to apply and how to work with it. Once they get that feeling of confidence, it can be done in the home, where it is much better for the patient.

Mr. FOGARTY. That sounds like progress, does it not?

Dr. WATT. Yes, sir. It is a very exciting program one that I think they are very rightly proud of.

Mr. FOGARTY. I assume it was started by someone in Georgia, who got this idea and developed it.

Dr. WATT. Yes, by Dr. J. Gordon Barrow, who is in charge of the program now. It was a development from the clinic program which began back with the earliest of the Heart Institute State grant programs. These clinics grew up over a number of years. They now have, I think, 18 scattered throughout the State which are used for, shall we say, continuing education. In other words, the physician can bring his patients in and they can have consultation on it whenever they want to. It is carried out as part of the voluntary health association, the Georgia Heart Association, and the State health department, on a collaborative basis.

A number of our young men in the technical assistance program have worked in Georgia, and it has given them invaluable training in this. We will be able through their experience to help other States in this same way.

HEART SURGERY

Mr. FOGARTY. You have made significant progress in heart surgery, too, have you not?

Dr. WATT. Yes. This field, of course, is the most dramatic of all, because the surgeon can actually repair the damage and you can see it, feel it, and touch it in a different way from other areas. I think it is important to point out that without the development that has gone on in anesthesiology, without what has been done in X-ray identification, none of these operations would be possible, because the surgeon could not know exactly what to do.

I was on a field trip just recently, and, at one of the projects I visited, the thing that intrigued me was the change that I have noticed over the last few years. On a laboratory visit about 6 or 7 years ago, if they had one oscilloscope showing some physiological phenomenon, they were very proud of it and showed you with a great deal of pleasure that you had helped them do this through the support of grants. Three or four years ago they began to have two things on the same oscilloscope. Now it is possible to monitor not one or two but, in some places, as many as four or five or six of these variables, such as blood pressure. The exciting thing is the way they are working on the little sensing heads which will tell you where these physiological variables measure on a continuous basis.

Down at the University of Alabama, they have some five experiments going on simultaneously, any one of which will be an important advance in terms of continuous monitoring of what goes on in the blood. If they can get four or five of these working together, this means we will really begin to understand what changes take place inside the heart and inside the body much more effectively. This will mean, too, that the surgeon will be able not only to do his operation but to follow up the results of the operation. That, I think, is one of the most important things we need to do now—long-term followup of these patients.

Mr. Fogarty. This followup program is becoming more important in every phase of medicine, is it not?

Dr. Watt. That is right. Its importance is increasing because we are increasing our ability to do something quite definitive and positive for the patient. When you were giving only symptomatic treatment or something of this sort, the followup was not so important; but when you take a definitive action, then it becomes crucial to know, do you really help over a long period of time, or only for a short period; and if it is for a short period, what can you do to improve it?

Mr. Fogarty. Mr. Denton will preside. I have to take a long-distance call.

Mr. Denton. Doctor, there are not a great many questions that I want to ask.

ANTICOAGULANTS AND CLOT-DISSOLVING DRUGS

Last year you talked about some experimental work on drugs to dissolve blood clots.

Dr. Watt. Yes, sir.

Mr. Denton. Is anything new being done on that?

Dr. Watt. Mr. Denton, this is one of the most complicated fields in medicine, as far as I am concerned. I find it very difficult to understand it. I can summarize my conclusions about as follows:

There are a very large number of factors which influence the speed and the completeness of the formation of a clot, and there are also a number of factors which tend to keep that clot from forming. Again, there are factors in the blood which will dissolve a clot, once it has formed, at least in its earlier stages. At the present time we have available substances which will dissolve clots, but it is very difficult to get them in such a form that you can predict from one time to the next just how effective they will be.

So we are dealing with a crude material rather than a refined one, and the work currently going on is being done not just by the Heart Institute but in industry quite actively to develop a standardized product which will allow for repeated experiments in the knowledge that the differences observed are due to the reaction of the clot and not to variations in the substance that you are using to dissolve the clot.

Mr. Denton. Of course, you can keep the clot from forming?

Dr. Watt. This is another type of drug we have now which is an anticoagulant, so-called, which will slow down the clotting process. This also is a little difficult to handle, because you need blood clotting. It is not always a bad condition. It is a good thing under certain circumstances. From just a cut finger, you would be in serious condition if you did not have something to stop the blood loss.

SURGICAL REMOVAL OF BLOOD CLOTS

Mr. Denton. What are you doing about operating to remove blood clots in case of strokes and other things?

Dr. Watt. Operations have been developed on that. I recently heard a surgeon talking about the much more effective operation that he could perform by using a special form of cooling of the brain. He puts the patient on a bypass; the patient's own heart is used but the blood is bypassed through a cooling machine. The cooled blood cools the brain down, and the surgeon can carry out his operation in a bloodless field much longer, much more effectively. They have been able to search out the actual point that the break occurred and do a repair job.

A number of patients have been improved markedly by removal of such a clot. It is a very laborious operation, and one that is not fully worked out, but successes have taken place and patients have recovered. I am sure that over a period of time the neurological surgeons will have made tremendous improvements on the current operation which does exist.

On a stroke itself I think it is important to keep in mind that complete recovery is common, particularly so if rehabilitation is early, if they begin to work with the patient immediately or very soon after the stroke so that the muscles are exercised. By the family working with them and doing these exercises, recovery is quite good and many recover with little or no residual damage.

Mr. DENTON. I imagine one of these operations must be performed very soon after the stroke to be effective?

Dr. WATT. Yes, for clot removal.

Mr. DENTON. Because the damage would be done if you did not get the clot removed?

Dr. WATT. That is right.

PREDICTING POSSIBLE HEART ATTACKS

Mr. DENTON. Some years ago I knew a man who went to one of the leading heart specialists in the community, and he was given a complete examination with electrocardiograph and everything the doctor had. The doctor reported he was perfectly sound, that there was nothing wrong with his heart. The man went out and walked two blocks and dropped dead. I think the man must have felt something was wrong or he would not have gone to have the examination, but the doctor found nothing wrong with him. I know of very fine heart doctors who examine a man and think he is all right and then we find out he is not. Has improvement been made in diagnosing possible heart attacks?

Dr. WATT. I think a great deal of progress is being made in a better understanding of what leads to a heart attack. I think as soon as this understanding is complete, nearly so, that we will be able to anticipate these problems. At the moment our devices for measuring what goes on inside an artery are very crude. In fact, it is almost impossible to do more than guess at the degree of damage that is going on in a small blood vessel. But there are devices, in X-ray, for example, now, where they can visualize the whole outline of the major coronary vessel and get a picture of the degree and extent of blocking of the blood vessels that is taking place.

Mr. DENTON. What kind of examination is that?

Dr. WATT. They inject a small amount of material that will be opaque to the X-ray and photograph it.

Mr. DENTON. Like a barium test?

Dr. WATT. Something like that. The difficulty with this test at the present moment is the danger of it. We have no material that can be injected in the blood vessels without some risk. You have to use it in very small amount and be very precise with where you put it or it gets diluted and you cannot see it. I imagine, analogous to the situation you spoke to me about yesterday, you said when you went to see Dr. Shannon they had a pacemaker about half the size of this room. I brought a small one here today. Considerable progress is being made in miniaturizing these devices.

Mr. Denton. About that machine we saw out there some years ago when Dr. Shannon was in the Heart Institute. He had a device that was measuring the heart beat. Was that a forerunner of this device we have here today?

Dr. Shannon. No, sir. What you saw was a machine that has never come into general use as a diagnostic instrument, although it still has a place, as it did at that time, in research.

Mr. Denton. Did you not have a big machine that does the same thing as this device?

Dr. Watt. I think they had a pacemaker at that time or shortly thereafter.

Mr. Denton. It was very large.

Dr. Shannon. That must have been 11 years ago.

Mr. Denton. Eight or ten years ago, yes.

Dr. Shannon. At one of the laboratories we visited there was a room—as I recall, it was one of the treadmill rooms—with gear that covered about half the wall and a variety of instruments to study the vascular system. This has not been miniaturized. What has happened, is that the complexities of these very extraordinary devices have been so simplified that they can now be used by people who are not electrical engineers. This has greatly increased the ability of the surgeon to know what he is doing at the time he is doing it.

Mr. Denton. This experience I was telling about may have happened 20 years ago, the one where the doctor said the man's heart was perfect and then he dropped dead with a heart attack. But I still hear of cases where people do not know they have heart trouble, and there seems to be a great deal of difficulty in diagnosing it.

Dr. Watt. Yes, sir; that is true. This is one of the things we have in our control program in Chicago. We are working with the American Heart Association there in developing means of recording the heart sounds and using them in the schools so that the physician does not have to individually first examine each child. They have developed methods of automatically screening and separating those who have normal sounds from those who have abnormal sounds and letting the physicians examine them separately after this screening. I think that will be a step forward in early detection.

Mr. Denton. You can tell if they have hardening of the arteries, can you not?

Dr. Watt. Provided it is in a location where we can get to it. We know that certainly all the men in this room have some degree of it. This much we can be sure of. The ladies are a little better protected, apparently, but all of us have some degree of it. The important thing is where it is and how we can control it.

Mr. Denton. I think that is all.

TREATMENT OF HEART DISEASE WITH DRUGS

Mr. Fogarty. Tell us about the development of drugs in the treatment of heart diseases.

Dr. Watt. This is a field that is very active. Mr. Fogarty. The industry has turned out quite a large number of them and we have had a very active program at Bethesda in studying the different types of drugs. I think the most important development has been in the field of monamine oxidase inhibitors in the last couple years.

Mr. Fogarty. Is there any other name for that?

Dr. Watt. They have some trade names. I guess the best way to call it is an enzyme which blocks certain of the ways the body handles the amines like adrenalin.

We have already developed a method which is speedy and simple, and which cuts down on the amount of equipment for detecting these materials, and based on our past studies we can do quite a good detection job. These drugs will lower blood pressure. Many of them apparently have an advantage over some of the earlier drugs used in blood pressure lowering in that they appear to have their action on the sympathetic half of the nervous system. The sympathetic and parsympathetic halves of the nervous system work together in the body and achieve a sort of balance. They block the action of both of these. It seems these inhibitors work on the sympathetic side and in general we do not have as many complications of the treatment as we had with the older blocking agents. These agents have some complications of their own, however, and it is a little soon to say how complete a drug that will be. I think they are good ones and I think progress in the study of them is going on quite well.

Mr. Fogarty. You do not have any program on chemotherapy, do you?

Dr. Watt. No, sir, we have no broad chemotherapy program similar to the Cancer Institute; no, sir.

Mr. Fogarty. Why not?

Dr. Watt. Largely because the pharmaceutical industry itself is spending so much of their energy and funds that I do not think it needs the same stimulatory action that was needed in the cancer field. We think we should go along with the collaborative studies and have the physicians better able to evaluate the effect of these drugs in their practice. The big difficulty now is there are so many drugs that it is hard to arrive at a base line for adaptation in the community.

EFFECT OF TRANQUILIZERS ON HEART PATIENTS

Mr. Fogarty. What about the use of tranquilizers on heart patients?

Dr. Watt. Many of the tranquilizers we have now grow out of studies in the field of blood pressure and adhesions, and this group of drugs has been important to men working in the heart field. Again, the studies of modes of action have been a major operation in Bethesda. This is one of the things we have paid particular attention to, and Dr. Terry was very active in this area before he decided to leave it.

Mr. Fogarty. I just wondered if they are helpful or harmful to a person who has had a heart attack.

Dr. WATT. There is no general answer, but they have been very useful to the physician in caring for the patients. These are very potent drugs and dangerous if used indiscriminately, but if properly used they are very useful.

Mr. FOGARTY. I am thinking more of the tranquilizers they sell in the drugstores. What are they called?

Dr. SHANNON. Miltown is one.

Mr. FOGARTY. Yes, Miltown is one. What are some of the others?

Dr. WATT. Miltown, I believe, is obtained only on prescription in most places. I do not know enough about the over-the-counter sales to know which ones are available by just walking in a drugstore. My own feeling is that all of them should be used with a great deal of caution and should be used for a particular purpose and not just a general purpose.

Mr. FOGARTY. Suppose a fellow was in a nervous condition, and he has had a heart attack, and the doctor says, "Take one of these a day"?

Dr. WATT. I think if the doctor prescribes it for him that is fine.

Mr. FOGARTY. Do you want to add anything, Dr. Terry?

Dr. TERRY. Nothing specifically except the use of those drugs have to be individualized to a patient. Certainly we have seen a patient with high blood pressure who, on being placed on tranquilizers or sedatives alone, has had a decrease in his blood pressure as a result of this particular thing.

We know also that periods of increased nervous tension also cause rises in blood pressure, put greater loads on the heart, and often a patient who has had a heart attack needs the protection of this sort of thing to relieve his anxiety and to keep him from exerting this increased load on his heart.

So I think these drugs do have a useful place in the treatment of cardiac diseases, but they have to be highly individualized.

GENETICS RESEARCH

Mr. FOGARTY. What are you doing in the field of genetics research?

Dr. WATT. We have a program on this in the Heart Institute laboratories and we have a number of places working on the understanding of how information is transmitted from one cell to another. I think this is the key to modern genetics, the determination of how small amounts of protein in one cell, when it divides, is carried over into the next generation of cells.

Mr. FOGARTY. Expand on that when you get the transcript.

Dr. WATT. All right.

(The following additional information was submitted:)

NATIONAL HEART INSTITUTE

ACTIVITIES IN FIELD OF GENETICS RESEARCH

INTRODUCTION

The NHI has strong interest in research in genetics because of the significance of knowledge accruing from this broad field to the mission of the Heart Institute for uncovering the causes of heart disease. The wide spectrum of genetics research support through NIH's general medical sciences program (which is the subject of another report requested by the committee) conveys its importance to the whole field of health and disease. The purpose of this report is to indicate the cardiovascular interest in genetics, the Heart Institute's support and conduct of work therein, and the meaning which progressing knowledge in genetics has and will have for the attack on heart disease death and disability.

GENETIC FACTORS IMPLICATED IN HEART DISEASE

Hereditary and genetic factors are among the major suspects—along with such others as fats, stress, sex factors, and exercise—as causative in the beginnings of such major forms of cardiovascular ailments as congenital heart disease, rheumatic fever, high blood pressure, and atherosclerosis. Familial or hereditary susceptibility has long been incriminated, for example, in rheumatic fever, which has been said to run in families. Similarly, genetic traits have been implicated in hardening of the arteries and consequent coronary attacks—and statements have been made that "one way to avoid a heart attack is to pick a line of ancestors who didn't have any."

While genetic factors as significant in proneness or susceptibility to heart disease have long been implicated, the gathering of both general and specific evidence on how when, where, in whom, and why this may be true requires not only a variety of basic and applied studies (ranging from the laboratory to populations) but also a range of time. Comparative studies of relatively short-lived animals are not alone enough to furnish the requisite information; studies in man himself, in families, in groups, in populations, are also necessary.

CONCERTED HEART GENETIC RESEARCH RELATIVELY NEW

It is today less than one generation since resources were first mobilized against heart disease through the creation of the National Heart Institute by the Congress. Thus, there has been a comparatively short span of years for cardiovascular genetic studies, particularly for those involving men on a long-term basis, to be designed, executed, and productive of comprehensive data on hereditary factors involved in heart disease. However, much has been learned, what is in effect a tooling-up period has been passed, and today there is growing interest while at the same time more scientific manpower is becoming available in the wide range of disciplines necessary to the many facets of genetic inquiry. Studies are possible of undertaking today which could not be done a few years ago; and the field is burgeoning.

HEART GRANTS IN GENETICS

Many of the research studies supported by the Institute have indirect bearing on genetics and involve some components related to hereditary factors in heart disease. There is, moreover, a substantial amount of work underway specifically directed to genetics through Heart Institute support from fiscal year 1961 funds. Some 18 investigations are being supported in the amount of $448,564. These are, of course, in addition to the support of genetics research through the Division of General Medical Sciences and through the disease-related programs of the other Institutes.

Heart supported genetics research is adding useful data, and thought not yet producing on a comprehensive scale, is beginning to emerge into areas of greater opportunity and to involve particularly interesting investigations. For example, two of this year's grants support studies concerned with red blood cell diseases found among U.S. citizens descended from persons in Greece and Italy; the research will include studies carried on in those countries to elucidate relevant genetic data. Other aspects of the international research activities of the Institute—including geographic pathology and population studies abroad—are also pertinent to the uncovering of information involving hereditary factors in heart disease.

Bearing also upon the question of genetics are recent findings from grants research in epidemiological studies. For example, a study of Negroes in the Bahama Islands reveals a high prevalence of elevated blood pressure. Comparison of the findings with the results of previous studies of Negroes in the United States and the Virgin Islands suggests that the blood pressure of Negroes is higher regardless of the geographic area studied or level of civilization. High salt intake and familial factors may be involved in the prevalence of hypertension in this Bahama population, the information shows. Additional dietary and genetic studies are being carried on to clarify the causes of this condition.

INTRAMURAL GENETICS RESEARCH

Intramurally, several studies are underway in Heart Institute laboratories bearing on the field of genetics, both at the basic level and with respect to hereditary factors in disease.

The basic studies involve experiments directed toward establishing how hereditary "information" coded into the genetic chromosomal material in cells is translated by the metabolic machinery into structures and properties that characterize individuals. The science of genetics thus aims to elucidate the mechanisms of heredity by describing, in molecular terms, the complicated processes that eventually lead, for example, to the development of individuals who are tall or short, dark haired or light haired.

The study of individual variations is very difficult with humans as mentioned earlier, because of the long generation times and lack of the proper experimental control. The studies being carried out in the Heart Institute at the basic level employ such organisms as bacteria and bacterial viruses which reproduce very quickly and on which, consequently, large amounts of statistics can be obtained in a relatively short time. Starting strains of such organisms are exposed to various agents which cause mutations, that is, changes in hereditary potential. The rsults of such hereditary changes are expressed in terms of the changes in such properties as rsistance to heat, or the ability to carry out specific biochemical reactions.

It is assumed at the present time that hereditary "information" is used by cells as a set of directions for the production of specific protein molecules which, in turn, perform the necessary functions of enzyme catalysis, hormonal action, and of furnishing structural material for building tissues. A single minute change in the genetic code, therefore, is expected to lead to a minute, but important, change in the structure of a corresponding protein molecule. The understanding of the relationships between the "genetic code" and the "protein code" is under active study.

At a higher level of cell organization the findings of the basic experimentalist in genetics are being applied to the study of human disease, an aspect of medical research which is receiving greater attention as investigators appreciate the frequency and importance of hereditary effects in medicine.

An interesting example is a newly discovered inheritable disease related to the transport of fat in the blood. Heart Institute scientists have tentatively called it Tangier disease because it was first discovered in a family on Tangier Island, Va. In this family the two children are missing one of the two major lipoprotein classes, known as the alpha lipoproteins. This seems to cause them to store tremendous amounts of cholesterol in their tissues. Each of the parents has about half the normal amount of alpha lipoprotein but enough to protect them from excesive cholesterol storage. This suggests that there are two paired genes for controlling synthesis of alpha lipoprotein and that the children have each inherited a defective pair of such genes. The role played by alpha lipoproteins in carrying fat in the blood and their relationship to the problem of atherosclerosis is an important area of research today, and study of this family should provide some extremely useful information.

CONCLUSION

In general, it can be said that heart research in cardiovascular-focussed genetics is progressing and emerging as an area capable of more concerted effort and support, with studies needed at many points along the range of research, from those into subcellular mechanisms to those delving into families, twins and other siblings, groups, racial factors, community, regional, or national populations. Today's evidence is that much may be expected from this area in the forseeable future to help establish useful knowledge about the causes of heart disease that will lead to measures to control those causes.

INTERNATIONAL RESEARCH

Mr. Fogarty. Will you supply a statement for the record of what you are doing in international research—what areas you are working in, how you are working with the specialists in other countries and what help they have been to your program.

Dr. Watt. Yes, sir; I shall be glad to.

(The information requested follows:)

NATIONAL HEART INSTITUTE

INTERNATIONAL RESEARCH ACTIVITIES

INTRODUCTION

The international activities of the National Heart Institute represent a broad and developing program. They form a significant part of the total Institute program and one that is brand new heart knowledge to our shores as well as sharing with our neighbors abroad the benefits of health knowledge that advance the cause of peace.

Both the direct operations conducted under the Institute appropriations and the activities supported by grants reflect the substantial needs and opportunities which international participation in research affords for developing cardiovascular knowledge which is helping and will increasingly assist in the attack and conquest of heart disease. In general terms, the Heart Institute's participation consists of activities in research studies themselves, research training, and the interchange of research knowledge. There is close integration with similar activities of the other Institutes and with the overall National Institutes of Health international programs under coordination of its Office of International Research Activities.

OPPORTUNITIES: DIRECT OPERATIONS AND GRANTS

The research activities of the Institute itself are substantially involved, since the research conducted by the Heart Institute is a natural part of the American and the international scientific community—and, in particular, that component of it which is especially concerned with heart disease. This is, of course, also true of Institute grants programs.

The international scientific community is also concerned because although heart disease is sometimes mistakenly thought of as especially affecting the United States far more than others, there are many countries heavily burdened with this disease complex. Thus, others are not only interested in scientific heart information produced here, but are themselves delving deep into its basic and clinical aspects. Therefore, it is worthy to note that research knowledge, which will benefit our citizens as well as those of many other countries, can well eventuate either here or abroad.

Moreover, it should be stressed that beneficial knowledge becomes all the more likely when there is brought to bear upon the vast problem of heart disease the combined talents of our scientists and those of other nations. Such is the rich opportunity which confronts us today.

One of the major means of seizing this opportunity is the development of collaborative cardiovascular research centers, involving direct operations and grants in partnership with other countries. Planning and execution of this type of activity is progressing well. By such means; by regular and frequent communication and interchange of already trained personnel and information; and by other methods, including research training and related activities, the large and growing opportunities to speed up the conquest of heart disease by work around the world may be taken advantage of.

DIRECT OPERATIONS PARTICIPATION

Currently, the Heart Institute's direct operation in international research take a number of forms, including the exchange missions with Russia. Hundreds of scientists from abroad visit for short terms or work for longer periods in Institute laboratories. Staff members are sent to other shores to study, to conduct collaborative work, or to present research findings and demonstrate techniques of ours. All of this serves to encourage the transmission of useful information and partnerships in research that will advance cardiovascular knowledge in ways not otherwise possible.

Some illustrations of this participation indicate its range, productivity, and promise. The heart intramural research area has a very active international visiting program in which scientists of foreign countries work in NHI laboratories. Scientists at all levels of experience and accomplishment, from junior fellows to the most distinguished investigators, come to exchange knowledge and techniques; engage in collaborative research projects; and utilize NHI facilities.

At present, the heart intramural program has 21 foreign participants representing 14 different countries.

As space and other facilities permit, NHI investigators accept in their laboratories guest workers who have their own funds. They may wish the experience of working with a specific investigator, or they may have a project that would be best accomplished at NHI.

Some of these guest workers are senior investigators on sabbatical leave from their universities. Many are young scientists on fellowships eager to advance their training in an area of specific interest to them or with an investigator at NHI who has renown in the field they wish to make their own. In exchange for the training they receive and the space and equipment they use, they bring the latest philosophies and techniques of the laboratories from which they come. At present NHI has eight guest workers from seven different countries—Brazil, Denmark, Italy, Scotland, Spain, Switzerland, and England.

As another illustration of NHI staff participation, within the past year intramural investigators have been invited to a scientific program in which they pursue collaborative programs with scientists in countries in which Public Law 480 funds are available. Investigators of the intramural program have one project underway with a scientist in Israel, and other projects pending final arrangements in India, Brazil, Colombia, Uruguay, and Indonesia. Three NHI senior investigators are interested in this type of collaborative study, and further interest will evolve.

Two other NHI scientists are scheduled to participate in the U.S.-U.S.S.R. scientific information exchange. NHI's chief surgeon is accompanying a cardiovascular disease delegation to visit surgical centers in Russia in May and another staff member has been requested to head a genetics and metabolism mission scheduled to visit Russia for approximately 3 weeks in October of this year. With no previous knowledge of the language, he has learned enough to present his report in Russian and answer questions. NHI has received three delegations from Russia visiting under the sponsorship of the exchange program.

The informal exchange of scientific information on an international scale is a continuous one. Scientists in the same fields of interest from all parts of the world correspond, exchange papers, and when possible meet with each other to discuss the progress of their research and to assist each other. This exchange is well exemplified by a young NHI investigator, Dr. Robert S. Gordon, who developed a diagnostic procedure to identify a disturbance of gastrointestinal function leading to low serum albumin levels. The substance used for the diagnosis is I^{131} polyvinyl pyrrolidone (a metabolically inert synthetic macromolecule) which, when administered intravenously to patients with gastrointestinal protein loss, "leaks" into the intestine and is detected in the feces.

Investigations with this substance have made it possible for scientists to demonstrate that internal loss of plasma proteins occurs in a number of recognized gastrointestinal diseases and this loss is largely responsible for the hypoproteinemia which so often accompanies digestive diseases. Dr. Gordon's publications describing I^{131} PVP brought requests for the substance from investigators in all parts of the world. In response to these requests, Dr. Gordon, in collaboration with the radiopharmaceutical service of the Clinical Center, has been producing and sending I^{131} PVP to investigators who need it in their research. The material has been shipped to at least 15 different countries, with shipments rising to an average of 2 a month. It is expected that within the year I^{131} PVP will be commercially produced and it will be possible for Dr. Gordon to discontinue production without causing delay in this important area of research.

THE EXTRAMURAL PROGRAM

The program of research grants to other countries supported by the National Heart Institute includes 97 grants to some 27 different countries. Of these, 67 awards are currently active and 30 others have been recommended for approval by the National Advisory Heart Council. The total from fiscal year 1961 funds is $1,443,000. It is interesting to note that this support is rather widely distributed among the countries, with only four of them receiving eight or more grants.

The 97 grants are in the following fields and the number in each is indicated in parentheses: arteriosclerosis, including geographic pathology and blood-clotting problems (39), blood and blood diseases (13), hypertension (8), other cardiovascular diseases (8), pulmonary and renal diseases (11), basic research of cardiovascular interest (16), worldwide medical abstracting journals (2).

The funds recommended for approval by the National Advisory Heart Council as of April 1 for fiscal year 1961 foreign program represents 3.4 percent of the present NHI appropriation.

NATURE OF ACTIVITIES ABROAD

The projects supported by NHI funds abroad may be either for individual studies of a somewhat limited nature or for large scale cooperative studies. Consequently, they may be carried out either independently, or in collaboration with U.S. investigators, or sometimes on the basis of a closely supervised joint protocol.

Occasionally, a study may start as an individual effort, then grow into a collaborative one. At other times, a joint research plan is first developed, and then individual participants are invited to join. An example of this latter is Dr. Ancel Keys' project designed to elucidate in various countries the relation of dietary factors to atherosclerosis. Another is the Cooperative United States-United Kingdom study under Dr. Donald D. Reid of London, designed to compare the form and occurrence of cardiopulmonary diseases in England and the United States. An individual study example is that of a Japanese investigation of "Atherosclerosis, Under a Low Fat Diet."

Another collaborative project between U.S. and foreign investigators is the pathology study centered at Louisiana State University (Dr. McGill) with collaborators in 13 Latin and Central American countries. These investigators aim to determine from post mortem material the onset and course of cardiovascular disease, and also its sex and race distribution.

New projects are also being planned. For instance, Tulane University (Dr. George Burch) is planning to study the unusual heart muscle damage (so-called enlarged heart) among the natives in Kampala, Uganda.

For another example, a new program of demonstration team visits to South American centers is being organized as a result of requests for information on the use of heart-lung bypass techniques in heart surgery. Full teams, some members of which can speak Spanish, will set up diagnostic, operative, and postoperative programs using portable equipment and demonstrates their use and the problems involved.

The National Advisory Heart Council has recommended four training grants (two in Scandinavia and two in England). These will support U.S. scientists wishing to have experience in particularly worthwhile or unique training opportunities that are not duplicated within the United States.

The foreign fellowship program of NIH helps to finance the training of a number of foreign postdoctoral scientists in institutions in the United States. For fiscal year 1961 there have been 84 fellows coming from 28 countries, and many of these have strong cardiovascular or cardiovascular-related research interests.

CONCLUSION

The above sketch of National Heart Institute participation in international research activities, of benefit to the mission of the Institute for cardiovascular research, shows that this participation, while a minor part of the heart appropriation dollar, is an expenditure of particular significance and worth in view of the returns it is bringing and will bring in knowledge useful to our citizens and to others.

Knowledge is being gained and interchanged concerning new surgical techniques, other therapies such as drugs, diagnostic and testing procedures, and epidemiology and geographic pathology. The regular and frequent exchange of scientific information—and the interplay of communication among both young and established scientists here and abroad—are widening and accelerating the development of basic and clinical cardiovascular knowledge. These things are also helping, directly and indirectly, as they proceed as a scientist-to-scientist community activity, in the very real and sound furtherance of health for world peace among the whole community of nations. The future of National Heart Institute international research participation, as that of the several Institutes and the family of NIH, is one of burgeoning promise.

DISSEMINATION OF MEDICAL INFORMATION

Mr. Fogarty. Are the funds for public dissemination of information on the discoveries in the heart disease field adequate?

Dr. Watt. We have a program in that which has been intensively looked at by the Council in the past year. Mr. L. E. Martin, who was with the Heart Institute some years ago and then in Dr. Shannon's office, is now back in the Institute as a special assistant to me in developing plans in this field.

At its November meeting, the Council recommended a step which one of the members commented was one of the most exciting he felt had been taken by the Council. This recommendation was that the Heart Institute collaborate with the National Library of Medicine in developing a means of screening scientific literature and providing the scientists with better reports on what existed. We have been working with Dr. Rogers in this respect.

As to public information, we feel there is a great deal of information going to the public and we are doing a lot to encourage it.

I might put in a personal comment at this moment. Some years ago I did a television show reporting on research findings which I stopped just because I did not have the time to keep on with it; it was twice a week. We are going to start it again on the second of April. This time, though, it will be on another station with time that will be a little easier to handle, and with the development of the video tape procedure I think I can work it out. We will try to have a weekly report that will be televised on Sunday afternoons. The first two programs have already been taped, and I might say the first one will be on this little artificial pacemaker that you saw this morning.

Mr. Fogarty. I have had some complaints that we do not get this information to the places where it can be used quickly enough and that you need some help.

Dr. Watt. I believe that the field is one that can be pushed now. I think we have information which would be extremely useful to people and I think there is a lot that can be done.

Mr. Fogarty. Why do you not supply for the record just what your needs are in order to do a better job of informing the medical profession as well as the general public of the progress in heart disease research, and how much you think you can effectively use in that area to do a better job.

Dr. Watt. I am sure this would be included in the request you have asked me for using additional funds. This would be a very important item in that.

Mr. Fogarty. Mr. Laird.

CAREER PROFESSIONAL AWARDS

Mr. Laird. Dr. Watt, on page 176 of your justifications you make a reference to the establishment of career professorship awards.

Dr. Watt. Yes, sir.

Mr. Laird. I would like to find out a little about this. Is this just a direct grant to medical schools to help them finance their faculties.

Dr. Watt. No, sir. To put it in my words, I would feel this is an award to an individual through a school or to the school for an individual to permit the stabilization of a research career. It is in a sense to make some room at the top for people doing research so that there is a place for them to carry on the type of work they have been trained for and to do so with some degree of certainty that they can plan ahead.

MORAL COMMITMENT OF NIH TO CONTINUE THE AWARDS

Mr. LAIRD. How do they plan ahead with this sort of grant which is only good for one year?

Dr. WATT. Mr. Laird, the custom has been over the years to award grants for a single year but with a commitment based upon the recommendation of the Council as to how long this would be continued.

Mr. LAIRD. What kind of commitment can that be? You cannot commit the Congress.

Dr. WATT. That is true, sir. We can do the work with the kind of moral commitment we have had in our program all along.

Mr. LAIRD. Is this a moral commitment from the standpoint of the Congress?

Dr. SHANNON. If I may answer, this is a moral commitment to give him an opportunity to do research and to give his program a high priority. We have been told by this Appropriations Committee and by the Senate Appropriations Committee that it is their intent to maintain a stable program in this area and that we were to conduct our program on that assumption.

Mr. LAIRD. But there is no moral commitment on the part of the Congress?

Dr. SHANNON. No, sir, none whatever. It is a commitment on our part that these individuals will be given high priority.

Mr. LAIRD. I would like to know what happens to these professors. Are they removed from the rolls of the universities and put on a special payroll? Just what are the details of the operations of this program?

Dr. SHANNON. The program was initiated this year with $2 million made available to establish it. The name of the program is the career research professorship program. The mechanics being developed to implement this program will permit medical and dental schools and related establishments to nominate for appointment a limited number of individuals who have achieved the scientific distinction to warrant the presumption that they will be productive contributors to science for an indefinite period of time.

Recommendations come to the National Institutes of Health and are reviewed by the Institute Advisory Committee, first, and by the Central Advisory Committee, second, in order to select those about whom the Council can feel secure in making an award.

The school, in addition to nominating the individual, will set a salary commensurate with his ability in a given field. The award will be made on an annual basis but with a commitment to continue that award for a 5-year period.

COMMITMENT FOR CONTINUATION OF SUPPORT

Mr. LAIRD. I want to understand this commitment for continued support. What kind of commitment can you make?

Dr. SHANNON. We can make a commitment of a very positive sort, I believe. If we cannot make these commitments we have no basis for running the program.

Mr. LAIRD. Legally what commitment can you make?

Dr. SHANNON. Legally, we can make no commitment.

Mr. LAIRD. What kind of commitment can you make?

Dr. SHANNON. The commitment is on the part of the National Institutes of Health to continue a given program at a given dollar level for a given period of time providing funds are available for its continuation. A small part of our total dollars is committed so that the grantee and grantee institution understand that even in the face of budget cuts it would be possible to continue the support of those programs for which we feel stability to be absolutely essential. In the absence of our ability to do this, we have no basis for the program.

Mr. KELLY. It is a moral commitment for the continuation of the program?

Mr. LAIRD. In other subcommittees of the Appropriations Committee, this same problem has been presented to us, and the Appropriations Committee historically has made its position very well known. As a matter of fact, we adopted a resolution in the last session of Congress which was approved by the full committee. It had to do with the area of foreign aid, but also other types of spending, and the sense of the resolution was that no executive agency could commit the Appropriations Committee or the Congress to the expenditure of any funds in years not covered by the budget.

Dr. SHANNON. The device I have just described in no way commits the Congress to appropriate a dollar.

Mr. LAIRD. I think it is a question of semantics. What you mean by "commitment" is not in the sense it is used by an Appropriations Committee?

Dr. SHANNON. No, sir. We have qualified this as a moral commitment by the National Institutes of Health to continue the program as long as funds are available for its continuation.

Mr. LAIRD. But it is not a moral commitment by the Congress?

Dr. SHANNON. None whatsoever, but I would say that an important element of our moral commitment is the understanding in the scientific community that the Congress does not look upon these programs as being of a short-term nature and that they will not be handled in a frivolous manner. They feel that they are operating within the stable intent of the Congress. But we do not commit the Congress to this.

Mr. LAIRD. I think time has shown that is the case and probably will be the case in the future. I do not quarrel with that, but I do not want to get in the position where it appears that there has been a change in policy as far as the Appropriations Committee is concerned.

Dr. SHANNON. No, sir; this concept of a moral commitment by the National Institutes of Health has been a guideline of our operations since we first started our operations in 1945.

SIZE OF PROGRAM

Mr. LAIRD. How many awards have you made?

Dr. SHANNON. We have put none, sir. We have had two groups of nominations for consideration. The first group consisted of 132 or

133, but after the Institute Advisory Committee and the Central Advisory Committee sorted through them, the number of wholly suitable ones came down to between 20 and 25. I do not recall the precise number.

The second group was submitted for consideration with a deadline of March 1. Staff work is now in process to prepare them for review.

PROBLEMS INVOLVED IN MAKING AWARDS

In the course of going over these applications, and in discussions with the schools and universities who have submitted the applications in the last 4 or 5 months, we have come to the conclusion that we have not developed guidelines that are sufficiently stable to permit us to say that this is the way we would choose to pursue it as a long-range program.

The difficulties that have arisen in planning the best use of these funds and the objections that have been made by the schools are:

First, the full use of these funds requires a commitment on the part of the school for long-term employment of the professor. We feel that, as a national agency, we can make no commitment as to tenure. Many schools have rigid regulations that prevent their making long-term commitments for full support to the individual over a substantial number of years. Other schools, particularly those that get their basic appropriations from the State, have regulations that preclude commitments on the part of the universities without an appropriation request prior to their making a commitment. In such a situation, and in the absence of full support for the maintenance of the commitment, the institutions have been unwilling to nominate the people who would be most suitable for this program. The bulk of the institutions which have not submitted names are waiting for the institutional grant. This would give them fluid funds in the research area, so that if the National Institutes of Health felt an individual could not qualify within the very rigid guidelines involved in a national program, it would permit them to support this professor's salary on a long-term basis, out of the more fluid funds.

The second major objection we have run into is in the very term for the award, which indicates that we are designating professors on a national level. They feel that it is quite improper for a national body to enter into the selection of a faculty member at a given administrative level, and they say that, as a matter of principle, they cannot participate in a program whereby their faculty is appointed by a national body.

The third problem is that it appears from discussions with the schools that the information material concerning the nominations of these individuals, has been interpreted differently by different schools. Some have nominated a senior investigator, well trained in research, around the age of perhaps 40, who has a distinguished career in retrospect and in prospect, but, because of limited funds, has a salary wholly derived from grants. This is the individual whose career we feel must be stabilized as an example to the young people who can be convinced that broad support of medical research is providing stable careers in research for the sake of research itself. This is the type of thing for which this award is ideally suited.

On the other hand, we have had a number of applications for professorship awards that would be more suitable for awards in recognition of a very distinguished career, such as are made by the Atomic Energy Commission.

Finally, we find that the schools themselves, have not been able, in their own plans, to provide for this new type of individual whose time will be spent substantially in research and only incidentally, or to a slight extent in undergraduate training, but who will be heavily involved in graduate-level training. It is impossible for them to work out sound mechanisms whereby this type of individual can be smoothly integrated into the faculty structure.

Mr. LAIRD. I should think it would be impossible to do that unless the grant were made to the school.

Dr. SHANNON. The grant is made to the school. The grant is applied for by the school and made to the school but in the name of the nominee they propose.

Mr. LAIRD. I thought you were making the grant to a specific person.

Dr. SHANNON. But the school nominates the individual. We deal wholly with the school and not at all with the individual. In other words, an individual cannot apply for such a grant. This program involves an institutional commitment of long-term tenure indicating that this school will provide a permanent place for this individual.

CONSIDERATION OF MATCHING PROVISION

Mr. LAIRD. Have you given any consideration to putting this on a matching basis?

Dr. SHANNON. We have not, sir. In our regular grant program, if an individual is a distinguished scientist, he can apply, or a school applies, for his total salary. What this does is to substitute a mechanism that is more suitable to permanent employment by a school than the annual, biannual, or triannual research grants.

Mr. LAIRD. What this is, is a followup of the American Cancer Society's program and the Heart Association's program. They obviously do not have enough funds to finance this program, and you are supplementing that type of program?

Dr. SHANNON. We hope to do more than that. One of the major difficulties of present programs is the failure to provide adequately for the individual in terms of his salary and support. It makes them an isolated individual in the academic society and makes it impossible for them to become an effective part of the academic structure.

I might say, Mr. Laird, that a number of schools now have decided that these grants cause sufficient difficulty, that they can no longer accept them. However, we do not feel that, at the present time, we have worked out the problem sufficiently well that our selection procedure and administrative regulations are such that if this Appropriations Subcommittee, and the Senate Appropriations Subcommittee asked us how much more we would like to have for this program, we would be able to say we could use no more than is in the present budget. I think our selection process and procedures at the present time must be considered to be experimental, and I have no certainty whatsoever, and as a matter of fact I have serious doubt that we can effectively use more than the $2 million earmarked for this program in the next fiscal year.

Mr. Laird. What do you think the attitude of the school is? Do you not think some of them would rather have just a straight grant which would let them make the determination?

RELATIONSHIP TO INSTITUTIONAL GRANT PROGRAM

Dr. Shannon. I think they all would agree that if there were some way of letting the institutional grant take complete care of this, that this would be a solution to their problem. This mechanism would be wholly ineffective in improving scientific excellence of many medical schools which do not have a sufficiently broad research program at the present time to compete successfully, via any institutional research grant program for funds to support this type of individual.

In other words, the institutional research grant, as proposed to you at the present time, would be a lump sum determined by three factors: one, a base grant of $25,000; two, would be a proportion—I believe the figure is 4 percent of the total value of the grants they compete for successfully within the Federal structure; and three, would be double that proportion of the value of the grants they compete for successfully in the private sector. Under the formula, many of our schools would have too little money to make effective use of these funds for the appointment of one or more of the type of professors we discussed

RELATIONSHIP TO GENERAL AID TO MEDICAL SCHOOLS

Mr. Laird. How is this type of program going to fit in with the overall medical school aid program which has been discussed?

Dr. Shannon. I do not believe it affects it one way or the other. I think this is just supporting stable scientists by a technique other than a research project by which we are able to support them now. This just provides stability of tenure rather than ad hoc support.

Mr. Laird. It seems to me there would be many schools that would have some difficulty with this kind of program because of the manner in which professorships are handled by their regents and trustees.

Dr. Shannon. Yes, sir.

Mr. Laird. I would question whether this type of approach would be equitable throughout the United States.

Dr. Shannon. As I said, many of the schools have not had the time or opportunity to discuss this with the faculty groups, boards of trustees, boards of governors, to the point where we know the extent to which the difficulties you suggest obtain.

In many cases the proposal of the schools to their board of governors is going to be that the regulations governing the appointment of professors be modified to the extent necessary to take advantage of this type of mechanism. Not only the research professorship, as defined here, but many uses of funds in the institutional research grant that we have proposed will require some modification of the rules and regulations to enable faculties to handle them.

Our feeling at the present time is that we should proceed very slowly with this program. We in no way wish to impose undue pressures on governing boards or faculties so that they are pushed into unwise decisions simply to take advantage of the small program that may be available to them.

They agree with us, however, that the most pressing need in the research area today is, in one way or another, to stabilize the salaries of their senior scientists. This cannot be done within the normal tenure systems that are available to most medical schools, and many schools today are addressing themselves to the problem of how this can be done. I do not think that the availability of this program itself has been the trip mechanism that set off this inquiry; this is something that has been continuously under study during the last 2 or 3 years as the most critical need to date that has not been solved by the schools.

RELATION OF CHOLESTEROL INTAKE TO AMOUNT IN THE BODY

Mr. LAIRD. Dr. Watt, I read with interest a report carried in the New York Times, a report made by Dr. Donald S. Frederickson, research associate at the National Heart Institute, in which he made the point that—and I quote: "The amount of cholesterol in the diet is of no importance because you cannot eat enough cholesterol." What do you think of that statement?

Dr. WATT. I think it is an oversimplification, Mr. Laird, of a very complex problem which probably was made in a general description of the problem we are dealing with. Certainly, it is true that cholesterol in the diet is not essential to the human being for having enough cholesterol in his body to get along. We can make it and we do make it.

In the normal course of events, we make more of it than we take in. It has been shown with some people that going on a relatively low diet will only temporarily reduce the cholesterol because they apparently make or their own body compensates for it. I have not seen the article. I do not recall the actual article you refer to. However, my feeling would be that it is a matter of relativeness within a particular problem he was discussing.

Dr. SHANNON. The amount of cholesterol which is actually formed in the body, as compared to the amount ingested in the average diet, is about 4 to 1. So that if you drop all cholesterol intake, you would drop the total amount of cholesterol available from five units to four units; if you doubled cholesterol intake, you would increase the cholesterol available from five units to six units.

The figure of four gives the general order of magnitude of what is produced inside as opposed to what is ingested and, of course, that will vary quite markedly with the diet. I think it is in this sense that the statement of Frederickson should be taken.

Mr. LAIRD. He also stated that no direct relation between the transient free fatty acids and coronary disease has been shown. Is that correct?

Dr. WATT. This is a matter of a great deal of intensive research at the present time, Mr. Laird. I think it is fair to say we do not really know the interrelationship of these different things.

CONSTRUCTIVE GRANTS UNDER SECTION 433(A)

Mr. LAIRD. Dr. Watt, your Institute has been using the provisions of section 433(a) of the Public Health Service Act.

Dr. WATT. Yes, sir.

Mr. LAIRD. You have used it the last 2 years, have you?

Dr. WATT. It has been used actually, Mr. Laird, only 1 year. We expect to use it this year. Last year we used it for the award of the grant to the University of Oregon for the Primate Center, the first one started.

The reason I qualify it for this year is we fully intend to, but the Council has not yet met and acted upon the applications we received; so that so far this year it has not been used, but the funds were appropriated with the intent of using it this year in the primate research facility.

Mr. LAIRD. I understand that in the new legislation which the administration has sent to Congress that the Heart Institute is covered but cancer is not. Is that correct?

Dr. SHANNON. That is correct, sir.

Mr. LAIRD. So that the programs that are presently in progress, as far as the Heart Institute is concerned, would be taken care of through a new section.

Dr. WATT. That was my understanding, Mr. Laird.

Mr. LAIRD. Do you find that you have need for a program along the lines of the program for cancer research facilities that the Congress approved last year?

Dr. WATT. Mr. Laird, there is a general need for additional research facilities. It has been our feeling so far that the Research Facilities Construction Act was providing research facilities for the cardiovascular disease and thus fitting it in with the school program quite satisfactorily. I had not felt that it was necessary to have special use of this except in the case of a particular type of resource like the primate facilities.

Mr. LAIRD. Your problem in heart is not the same as cancer?

Dr. WATT. It is a different problem, yes, sir, in the sense of the type of way you can attack the problem as well as the types of investigators who will be working on it in a given university situation.

My feeling is that the general grant program by and large will satisfy the bulk of the heart needs, although there will be special cases in the case such as primate research facilities where such general authority would be needed.

Mr. LAIRD. You believe that any primate colony construction under 433(a) should not be tied to one single university or medical research institution, that it must be regional in scope?

Dr. WATT. That is correct. This is the only basis on which we have studied this problem. We felt any individual laboratory facilities could be supported on a general research facilities construction grant. In fact, I am sure, without knowing the facts, I am willing to state now there are primate facilities that have been built on the general research facilities construction program one way or another.

Dr. SHANNON. There have been a fair number of animal facilities, and I would assume that some of these are for primates for the use of the individual institutions.

Dr. WATT. This is the assumption I made when I said this.

Mr. LAIRD. It was my understanding that the problem that faced you is somewhat different from the problem as far as cancer is concerned.

Dr. WATT. Yes, sir.

Mr. LAIRD. I was surprised to learn, though, that you felt that this proposed legislation which we have would take care of all your needs.

Dr. WATT. Mr. Laird, I have not gone over the bill in detail. I have had occasion to look into the specific effect on these primate facilities. I can only say that in terms of construction this Research Facilities Construction Act has been a tremendous value to us in the heart program. I feel it is an essential part of the development of the program. It is no question that the acute need in this country is for additional research facilities. I believe these can be furnished us through the General Research Facilities Construction Act in the main.

PROBLEMS OF MATCHING

Mr. LAIRD. You have no places that are having difficulty in raising matching funds for heart research facilities?

Dr. WATT. Yes, sir, there are a lot of them having trouble raising matching funds.

Mr. LAIRD. Is the program being held up any by it?

Dr. WATT. We have one particular case that is very important to us in the sense of being more a matter of carrying out our collaborative activities. That is our Baltimore City Hospital Laboratory. There is a problem of some difficulty in this respect. The problem there is not so much the abilities as it is the fact that we are working out a collaborative program in which our own intramural scientists are actually physically located and working in Baltimore. There is a problem of very real magnitude to us. I believe this can be handled under this new proposal.

Mr. LAIRD. That could not be handled under the new bill, the new proposal we have before the Congress at the present time, because that would not be regional in scope. Is that not true?

Mr. KELLY. I do not know. I am not familiar with it.

Dr. SHANNON. I think, Mr. Laird, it probably would. This is a peculiar situation that is quite abnormal.

Here is a Federal operation, fully supported federally, for which facilities are provided by the city of Balitmore, which is adjacent to a broad program within Johns Hopkins University with Johns Hopkins' personnel assigned full time to Baltimore City Hospital where their work is in large measure supported by our grants, and where, again, the research facilities are provided by the Baltimore City Hospital.

The solution of this problem could be in any one of several ways. The city of Baltimore could deed to us such ground as was necessary for us to build a building for direct operation in Baltimore, and we could run that and invite the collaborating group from Hopkins to occupy part of the space. This would not be an unconventional type thing.

Or if Hopkins considered that this was sufficiently important to them as an institution themselves, they could apply under the research facilities construction. Or if this were designated as a laboratory of national importance—and it is in fact the only comprehensive research laboratory in Baltimore—and it was determined to set this up as one of the limited number of national centers, then it could qualify under the new legislation.

Mr. Laird. You mean under this proposed new legislation you could go around doing this sort of thing all over the country; is that right? I would like to have this clear in my own mind.

Dr. Shannon. I am saying it is conceivable that it could be done this way. I can think of no other situation that has the complex set of variables that obtain at this particular laboratory.

Mr. Laird. Take one with which I am familiar, the McArdle Clinic. That takes care of all Wisconsin. Is that what you mean by regional in scope?

Dr. Shannon. No; this would be one of a limited number of laboratories designated as national laboratories, much the same way as Brookhaven, Oakridge, or one of the others.

Mr. Laird. You think under the new bill you could finance those 100 percent?

Dr. Shannon. I do not believe we would propose it, sir, but I think the answer is yes, we could.

Mr. Laird. You would not propose it?

Dr. Shannon. I would not want to commit ourselves at this point in time but, as I see it, this would not be a normal proposal. I think what we would do here is to apply for funds within our direct appropriation for direct construction, since a substantial amount of the building would be utilized by our own intramural research. I think this would be the cleanest way to do the job.

Mr. Laird. That is all I have.

GEOGRAPHICAL VARIATION OF CORONARY DEATH RATES

Mr. Fogarty. I have just one more question. In Public Health Reports of August 8, 1960, there is an article, "Death Rates per 100,000 population for Coronary Heart Disease in 163 Metropolitan Areas." It shows a great difference between areas, does it not?

Dr. Watt. Yes, sir.

Mr. Fogarty. Even within the same State.

Dr. Watt. Within the same State and between States.

Mr. Fogarty. The highest death rate from coronary heart disease is Savannah, Ga., with 826 per 100,000. That is No. 1. Charleston, S.C., is No. 2 with 825; and Galveston, Tex., is No. 3 with 802.

Dr. Watt. Birmingham——

Mr. Fogarty. Birmingham is not so bad. It is 517.

Dr. Watt. Montgomery is another.

Mr. Fogarty. What does this all mean?

Dr. Watt. I wish I knew the full answer to that, Mr. Fogarty. We have brought this to the attention of a number of city health officers. One of the objectives during the coming year in the studies that brought these figures out is to begin to look more intensively in these cities that have widely diverging rates and let the health officers and the vital statistics groups begin to work out what are the factors involved. There are certainly some possibilities of important information coming from this.

Mr. Fogarty. It says that coronary heart disease death rates are 37 percent higher for males and 46 percent higher for females in metropolitan areas than in nonmetropolitan areas.

Dr. WATT. These are some very intriguing figures, and there have been all sorts of speculations as to what might be the reason for it. I think we just have to say we do not know now, but we are trying to find out.

Mr. FOGARTY. I would think that we should put some more effort into finding the reasons for things like this.

Dr. WATT. It is a matter that the health officers themselves will go into.

Mr. FOGARTY. Maybe we will end up with your needing more than $50 million over your budget if we keep going this morning, Doctor. I can see several areas where you need more than is in this budget.

Dr. WATT. The most important thing here is to improve the basis on which the actual recording and analysis of these certificates are carried out. I think this is a project that has to be worked carefully with the Bureau of State Services, for example. This is the area they are principally concerned with. This is where this work was carried on, incidentally.

Mr. FOGARTY. Will you refer this article to them?

Dr. WATT. No, sir. Dr. Rikli, Chief of the Heart Disease Control program is already in on that. They are aggressively working on it now.

Mr. FOGARTY. I think we ought to do something in this area and do it as fast as it can be efficiently done.

Do you have anything else you want to say?

Dr. WATT. No, sir. Thank you.

Mr. FOGARTY. Thank you Doctor.

INCIDENCE AND COST OF HEART DISEASE

We will place the statements on incidence and cost, and highlights of research in the record at this point.

(The statements referred to follow:)

NATIONAL HEART INSTITUTE

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases dealt with in the National Heart Institute, and the estimated annual cost to the Nation.

I. DEATHS FROM CARDIOVASCULAR-RENAL DISEASES DURING 1959 (NATIONAL OFFICE OF VITAL STATISTICS)

Category:	*Number*
Arteriosclerotic heart disease (includes coronary disease or "heart attacks")	474, 143
Cerebrovascular lesions (includes strokes and other blood diseases in the brain)	191, 376
Hypertension	81, 278
Nonrheumatic chronic endocarditis and other heart muscle degeneration	56, 099
General arteriosclerosis	34, 622
Rheumatic fever and rheumatic heart disease	18, 290
Other cardiovascular diseases	42, 528
Total	898, 336

II. DISABILITIES FROM CARDIOVASCULAR-RENAL DISEASES (FOR YEAR ENDING JUNE 1958—FROM U.S. NATIONAL HEALTH SURVEY SERIES B–10, MAY 1959 AND B–13, FEBRUARY 1960)

	Disability category		
	Restricted activity	Sick in bed	Away from work
Number person-days of disability (in millions):			
All cardiovascular-renal diseases	497	173	72
Heart conditions	238	88	--------------
High blood pressure	99	32	--------------
Average number of persons (in thousands)	(1)	(1)	(2)
All cardiovascular-renal diseases	1,362	474	288
Heart conditions	652	241	--------------
High blood pressure	271	88	--------------

[1] Person-days/365.
[2] Person-days/250.

III. ESTIMATED ANNUAL COST TO THE NATION (FROM U.S. INCOME AND OUTPUT, DEPARTMENT OF COMMERCE, NOVEMBER 1958, AND VETERANS' ADMINISTRATION)

Compensation and pension payments to veterans disabled by diseases of the circulatory system totaled approximately $464 million in 1960. Lost productivity of those still in the labor force (item II–3, at estimated average earnings of $4,200) for 1958 is estimated at $1,210 million. Figures on expenses of hospitalization and other medical care are not available, nor any figures on which to estimate the productivity loss of persons no longer in the labor force (retired for disability).

Highlights of Progress in Research on Heart Disease 1960

(Items of interest on program developments and research studies conducted and supported by the National Heart Institute)

ATHEROSCLEROSIS AND CORONARY HEART DISEASE

MER–29 lowers cholesterol by blockade of final step in its synthesis by liver

Studies by NIH scientists have pinpointed the mechanism by which MER–29 lowers serum cholesterol levels. By blocking the conversion of desmosterol to cholesterol, the drug inhibits cholesterol synthesis by the liver at the very last step of the complex sequence of reactions by which the cholesterol molecule is formed.

These studies were made by Drs. Joel Avigan and Daniel Steinberg, of the NHI Laboratory of Cellular Physiology and Metabolism; and Mr. Malcolm J. Thompson and Dr. Erich Mosettig of NIAMD. Their findings are reported in Progress Against Cardiovascular Disease (2: 525–530).

The scientists observed that the sterol material in the livers of rats treated with MER–29 had properties that differed subtly, but definitely, from those of cholesterol, the major sterol of normal livers. Careful analysis revealed the presence of large amounts of desmosterol, a compound identical to cholesterol except for two missing hydrogen atoms at one point in the molecule.

When they injected radioactive acetate, a cholesterol precursor, into animals pretreated with MER–29, they found that most of the radioactivity accumulated in desmosterol rather than in cholesterol. Clinical studies also showed that desmosterol accumulated in high concentrations in the serum of patients receiving the drug.

These and other findings indicated that MER–29 lowers serum cholesterol by inhibiting the desmosterol-cholesterol conversion. They also help to clarify the process of normal cholesterol biosynthesis in man by providing factual evidence that desmosterol is an intermediate in this process.

In humans the most important source of serum cholesterol is not that consumed in the diet, but that synthesized by the liver, which readily manufactures cholesterol from fats, carbohydrates, or proteins—all of which can give rise to acetate, the primary building block. Thus the possibility of lowering serum cholesterol levels by the use of drugs which inhibit the body's own production of cholesterol has attracted increasing attention during the past few years. MER–29 appears to be the most promising of the compounds developed thus far.

The synthesis of MER–29 was announced in 1958 by Frank Palopoli and coworkers at the William S. Merrell Co., Cincinnati; and its cholesterol-lowering effects in rats were announced in 1959 by Thomas Blohm and Robert Mackenzie of the same company. The drug, also called Triparanol, is marketed by the William S. Merrell Co., who also made the drug available for clinical research.

The NIH clinical studies showed that MER–29 reduced serum cholesterol levels in patients without producing any observed toxic effects. However, the fall in serum cholesterol was accompanied by a rise in serum desmosterol, so that total serum sterol levels were not greatly changed, and were actually increased in some patients. The investigators suggest that the biological role of desmosterol warrants more thorough investigation, since information thus gained might be pertinent to the safe long-term use of drugs, such as MER–29, which might lead to the pileup of compounds normally present in the body only in very low concentrations.

Grantee study evaluates prognosis of victims of first heart attacks

An NHI grant-aided study of survival and factors affecting survival after the acute phase of first heart attacks (myocardial infarction) has shown that more than half of the 224 patients studied survived for 5 years or more. The 5-year outlook was brighter for younger patients than for older ones, was brighter for men than for women, and was brightest for patients able to resume normal activity after their attacks.

The prognosis of patients surviving for more than 1 month after their first clinically diagnosed heart attack was evaluated by Drs. J. L. Juergens, J. E. Edwards, R. W. P. Achor, and H. B. Burchell, of the Mayo Clinic, Rochester, Minn. The scientists determined the rates of survival for 224 patients 3, 5, and 10 years after the initial attack. They also evaluated statistically the effects on survival of such factors as age at onset; sex; preexisting angina or hypertension; congestive heart failure developing subsequent to the attack; occupation (active or sedentary); and degree of physical disability resulting from the attack. Their findings are reported in the AMA Archives of Internal Medicine (105: 444–450).

The average age at time of onset was 62 years (60 years for men, 67.5 years for women). Followup of these patients showed that 68.8 percent survived for 3 years or more after their attacks; 55.4 percent for 5 years or more; and 29.2 percent for 10 years or more.

Not surprisingly, 5-year survival rates were highest among those suffering attacks in their forties or fifties (78.6 percent and 62.5 percent), declined moderately among those having attacks during their sixties (to 56.6 percent), then more sharply among those having attacks in their seventies or eighties (to 25.9 percent and 20 percent, respectively). Also no surprise was the finding that preexisting angina or hypertension, or congestive heart failure developing after the attack, made the 5-year prospect bleaker—by about 25 percent on the average.

The study also indicated that 5-year survival rates were not significantly affected by the degree of physical activity involved in the occupations of male patients; were considerably higher for men than for women; and highest for those patients who were able to resume normal activity after their attacks. The better prognosis enjoyed by the men could not be fully accounted for either by age differences at time of onset or by any other factors observed in the course of the study. The excellent 5-year survival rate (73.2 percent) of patients who were able to resume normal activity after their attacks has also been observed in other studies, and appears to be the best index of a good prognosis.

Necropsy studies on 79 patients who survived their initial attacks but died later revealed that 82 percent subsequently died from cardiovascular disease. Of these, 34 percent succumbed to recurrent myocardial infaction.

Hyaluronidase reduces edema in ischemic heart muscle

The edematous fluid accumulations in heart muscle which follow coronary artery ligation in dogs, are markedly reduced by hyaluronidase injections, report Drs. J. Martins de Oliveira, M. N. Levy, and Mr. M. I. Schock, of St. Vincent Charity Hospital in Cleveland. Their NHI-supported studies are reported in the American Heart Journal (60: 106–109).

Dr. Martins de Oliveira and coworkers tied off a branch of the left coronary artery in 14 dogs to produce infarction and edema of the posterior papillary muscle (PPM). Eight of these dogs received hyaluronidase intravenously immediately after ligation and at hourly intervals for 5 hours, whereas the remaining six dogs received placebo injections of saline solution. Six nonligated dogs served as normal controls.

Specimens of the PPM and of anterior superior left ventricular tissue (ASLV) not affected by coronary ligation, were taken from the animals at sacrifice 5 hours after ligation. Differences in tissue water content, measured by comparing tissue weights before and after drying the tissues in an oven, were used as a simple, accurate index of edema formation.

From these studies the scientists found that PPM water content averaged 77.48 percent in the hyaluronidase-treated group, but increased to an average of 79.92 percent in dogs that received only placebo injections. ASLV values in both of these groups, 76.39 and 76.21 percent respectively, approximated normal control values obtained from nonligated dogs. The differences between normal and ischemic myocardium in the experimental groups are statistically significant, report the investigators.

"In the present study, hyaluronidase significantly reduced the water content of the ischemic myocardial areas, bringing it to values close to those of the normal regions," conclude the Cleveland scientists. However, they state, "The practical application of our experiments is still uncertain, since it remains to be proved whether or not it is beneficial to reduce edema in an ischemic myocardium. It may be postulated, however, that the increased tissue pressure caused by this edema may exert a compressive action upon the collateral vessels, thereby reducing still more the flow of blood to the damaged areas. Further investigations are now being carried out in an effort to answer this question."

Hyaluronidase, or "spreading factor," is a mucolytic enzyme used by physicians to promote diffusion and absorption of drugs injected subcutaneously. Recent findings by Hungarian scientists, who demonstrated that intravenous hyaluronidase produces a faster diffusion of fluids through extracellular spaces and enhances lymphatic drainage, provided the basis for using hyaluronidase in the present study.

Heart attacks treated by coronary injections of clot-dissolving enzyme

A technique using a cardiac catheter to inject the clot-dissolving enzyme fibrinolysin into the coronary arteries has been used by NHI grantees in the treatment of eight patients with myocardial infarction. The procedure, which was well tolerated by the patients, appears to possess two important advantages over oral or intravenous means of administering fibrinolytic therapy in such cases. It provides high concentrations of clot-lysing enzymes at the site of the clot without unduly elevating whole-system concentrations; and it allows intermittent perfusion, a procedure that appears to be more effective in dissolving clots than is continuous perfusion.

These studies were conducted by Drs. Robert J. Boucek and William P. Murphy, Jr., of the University of Miami School of Medicine, Miami, Fla. Their findings are reported in the American Journal of Cardiology (6: 525–533).

The technique involves passing a cardiac catheter into the aorta via the brachial artery and, under fluoroscopic guidance, positioning the catheter tip at the root of that great vessel. This brings the catheter orifice in line with the coronary branches, so that fibrinolysin injected through the catheter will be swept into these vessels with their blood supply. To assure that the fibrinolysin is delivered at the exact time that the coronaries are filling with blood, the injection is made by a small pump activated by the R wave of the electrocardiograph. Best results were obtained in this study when injections were made during every fourth cardiac cycle.

The patients selected were treated within 4–12 hours after onset of the attack. Because of its reported enhancement of clot lysis, heparin (an anticoagulant) was perfused with the fibrinolysin (as Thrombolysin: Merck, Sharp & Dohme).

The effectiveness of therapy was evaluated on the basis of the patients' clinical response; subsequent ECG data; and determinations of serum glutamic oxaloacetic transaminase (GOT), an enzyme released from injured heart tissue and which provides an index of the extent of heart damage. No attempt was made to evaluate clot lysis by angiology because it was felt that injections of radiopaque susbtances, which are somewhat toxic, might be harmful to heart tissue already hyperirritable.

The evaluation, through limited by available methodology, suggested that most patients were benefited by the therapy. All had an unusually mild clinical course in the hospital. All but two had serum GOT levels considerably lower than those of unperfused controls, indicative of less heart muscle damage. GOT levels were lowest in patients treated within 4 hours of the attack, highest in those treated 9–12 hours after. This indicates that fibrinolytic therapy, to be effective, must be initiated quickly, since it appeared that heart damage became irreversible about 4 hours after myocardial infraction.

While this study does not offer conclusive proof that fibrinolytic therapy is benefiical in the treatment of mycardial infarction, the technique used may prove extremely useful for future studies in this important, rapidly developing research area.

Androsterone linked to high serum cholesterol of thyroid deficiency

Androsterone, an important endproduct of the metabolism of certain male sex hormones (androgens) may be an important factor in the high serum cholesterol levels that usually accompany thyroid deficiency.

NHI grant-aided studies on the role of thyroid hormones in steroid metabolism have shown that androsterone levels in the blood are below normal in patients with thyroid deficiency and high in those with hyperthyrodism. The studies also showed that injections of androsterone produced a sharp and significant fall in the serum cholesterol levels of normal subjects and those with hypercholesterolemia. These findings suggest that androsterone, a metabolite of certain androgens, may be an important determiner of serum cholesterol levels, since these are usually elevated in hypothyroid patients and low in those with hyperthyroidism.

These findings are summarized in Annals of the New York Academy of Sciences (86: 605–611) by Drs. T. F. Gallagher, Leon Hellman, H. L. Bradlow, B. Zumoff, and D. K. Fukushima, of the Sloan-Kettering Institute for Cancer Research, New York.

Androsterone is one of two major end products from the metabolism of testosterone and certain other androgens; the other, etiocholanone, is structurally similar but differs sharply from androsterone in its biological activities. The scientists found that, in euthyroid patients (normal thyroid function), the ratio of androsterone to etiocholanone was 40:60. However, the androsterone fraction was only 15 percent or even less in patients with hypothyroidism from myxedema; conversely, it was 50 percent or higher in those with hyperthyroidism from Graves' disease, toxic nodular goiter, or toxic adenoma.

The scientists found that the androsterone fraction was sharply increased in euthyroid patients when they were given thyroid hormone, and was decreased toward normal in patients whose hyperthyroidism was corrected by therapy.

The cholesterol-lowering effects of androsterone might seem paradoxical, since the androgens from which it is derived are normally associated with high serum lipid levels. However, the scientists point out, hormone metabolites are not necessarily inactive end products of a spent hormone. They may have their own important physiological functions that are not related in any way to those of the substances from which they are derived.

These findings are the basis for an hypothesis, advanced by the scientists, that the recognizable effects of thyroid excess or deficiency are mediated by the availability of androsterone in the body. They also suggest that androsterone deficiency may be one of the mechanisms involved in the development of hypercholesterolemia and, perhaps, of atherosclerosis.

New technique provides more sensitive measure of plasma clot lysis

Using a sensitive, direct assay technique that closely approximates in vivo conditions, NHI grantees have measured the degree of clot-dissolving activity in human plasma. They report in the Journal of Clinical Investigation (39: 426–434) that such activity depends primarily upon an activator whose concentration in plasma varies widely in response to stress, certain drugs, and disease.

For these studies Drs. W. D. Sawyer, A. P. Fletcher, Norma Alkajaersig, and Sol Sherry, of the Washington University School of Medicine, St. Louis, prepared clots from aged human plasma enriched with plasminogen and containing traces of bovine fibrinogen tagged with radioactive iodine. The methods used produced I^{131} labeled clots that were largely free of entrapped human plasma.

The clots were then incubated for 2 hours at body temperature in samples of unaltered plasma from healthy adults who had been subjected to stress or pretreated with certain drugs, and from patients with various chronic or infectious diseases. The degree of clot lysis was determined by measuring the amount of radioactivity released into each plasma sample as the clot dissolved.

Thrombolysis is a complex process involving many factors whose exact roles have not yet been clarified. The major components appear to be plasmin, the enezyme that actually dissolves the clot; plasminogen, its inactive precursor; and plasminogen activator, which converts plasminogen to plasmin. The circulating blood is thought to contain inhibitors for both active principles so that, under normal circumstances, they are present in the circulation in their "neutral" forms.

A blood clot also contains plasminogen, which was trapped in the clot during its formation. In fibrinolysis, it is thought, plasminogen activator accumulates on the fibrin surface of the clot and proceeds to convert the trapped plasminogen to plasmin. The plasmin dissolves the clot from within by digesting its fibrin.

Further knowledge of this property of plasma and better means of measuring it have been made essential by recent developments in the field of fibrinolytic drugs. However, techniques heretofore available were indirect, were not sufficiently sensitive, or disturbed the complex balance between individual plasma components. The technique used in this study appears to avoid these limitations; and, with it the scientists have been able to provide experimental confirmation of concepts that formerly were largely inferential.

They found that plasma clot-lysing activity was sharply increased by sustained vigorous exercise and was increased by emotional stress or injections of nicotinic acid (a B-vitamin) or a fever-producing drug. It was also generally elevated in patients with acute infections, liver disease, or leukemia.

Conversely, clot-lysing activity was commonly observed to be below normal in patients with cancer other than leukemia, congestive heart failure, or atherosclerosis. This subnormal activity may be casually related to the thrombo-embolic complications that frequently attend these diseases.

Plasma clot-lysing activity was found to be due primarily to the plasminogen activator it contained, and upon the plasminogen in the clot rather than that in the plasma. Clot lysis was greatly reduced when clots containing little plasminogen were incubated in the plasma samples, and was practically nil when plasminogen-free clots were used. Clot lysis was also reduced by the addition of E-aminocaproic acid, which in low concentrations effectively inhibits plasminogen activator, but not plasmin.

Clot-dissolving enzyme isolated from thrombin by NHI grantees

Chemical "dissection" of thrombin has yielded a new clot-dissolving, or fibrinolytic enzyme identified as thrombin-E, report Drs. Walter H. Seegers, Ricardo H. Landaburu, and J. Frederic Johnson at Wayne State University in Detroit. The scientists observed powerful fibrinolytic effects of the new enzyme following its intravenous infusion in dogs.

Their findings published in Science (131: 726) stem from an earlier observation that thrombin, long known for its important physiological role in catalyzing the formation of blood clots, has both the power to form and subsequently dissolve fibrin clots under certain laboratory conditions.

In their currently reported studies, the investigators attribute the lytic activity of thrombin to a distinctly different enzyme which they named esterase thrombin, or thrombin-E, to distinguish it from thrombin-C, the parent compound.

They produced thrombin-E in pure form by acetylating thrombin-C with acetic anhydride. This destroyed the clotting power of thrombin-C and almost doubled the activity of thrombin-E, which was then stabilized by drying.

Dog experiments demonstrated the ability of intravenously infused thrombin-E to dissolve blood clots. In a typical experiment, 15 milligrams of dried thrombin-E dissolved in 100 milliters of physiological saline solution was slowly injected over a period of 1 hour and blood samples repeatedly withdrawn. Dr. Seegers and coworkers report that at the end of the infusion period, blood samples clotted but subsequently lysed within an hour. "Occasionally the lytic phenomenon was so pronounced that the blood would not clot spontaneously upon withdrawal or even after thrombin was added," they stated. The dogs tolerated the procedure very well: the few physiological effects observed, such as lowered platelet and white cell counts, increased blood sugar levels, and lytic phenomena, disappeared within 24 hours.

The investigators speculate that thrombin-E may function by activating physiological processes concerned with fibrinolysis and thus the maintenance of blood fluidity. "This opens possibilities for the useful application of thrombin-E," they said.

Arachidonic acid possible factor in resistance to atherosclerosis

Studies by NHI grantees suggest that arachidonic acid—a highly unsaturated fatty acid found in certain fish oils, dairy products, and fowl—may be a significant factor in the relative immunity to atherosclerosis enjoyed by animals of certain species. In these studies the cholesterol fractions of serum from man and from seven other species were analyzed and compared. The arachidonic acid content of serum cholesterol esters (which comprise about 70 percent of the total blood cholesterol) was found to be highest in those species most resistant to atherosclerosis, lowest in the most susceptible species.

The largest amounts of arachidonic acid were found in the cholesterol ester fractions of the rat (50 percent) and the dog (17 percent), both highly resistant species. Much smaller amounts (1.1–5.8 percent) were found in the cholesterol esters of the goose, chicken, rabbit, guinea pig, and pig. Severe atherosclerosis can be produced in these species by feeding them high-cholesterol diets for only a short period, even though they seldom appear to develop the disease spontaneously.

Man (7.5 percent) is susceptible to atherosclerosis, but usually develops severe lesions only after many years on a diet high in fat and cholesterol (although much lower in cholesterol than the atherogenic diets fed laboratory animals).

However, the scientists point out, these findings, though in accord with an hypothesis that arachidonic acid deficiency is an important causal factor in atherosclerosis, have not proved that arachidonic acid is the protective factor nor that more of it in the diet of humans will make them less susceptible.

But the possibility remains that the arachidonic acid content of human lipids may be increased by diets higher in this fatty acid or the elements from which it is synthesized (linoleic acid plus the cofactor vitamin B_6). It would then remain to be seen whether such an increase would confer upon man greater immunity to atherosclerosis.

These studies were done by Dr. Leon Swell, of the Veterans' Administration Center, Martinsburg, W. Va.; and Drs. Henry Field, Jr., and C. R. Treadwell, of George Washington University. Their findings are reported in Proceedings of the Society for Experimental Biology and Medicine (104: 325–328).

Find serum cholesterol not related to obesity in healthy young men

No significant correlation was found between serum cholesterol level and relative obesity in 159 male medical students at Johns Hopkins University, report Drs. Caroline Bedell Thomas, Johns Hopkins University School of Medicine, Baltimore, and Stanley M. Garn, Fels Research Institute, Yellow Springs, Ohio. Findings of their NHI grant-aided study appear in the journal Science (131: 42).

Obesity measured indirectly was expressed in the study as actual weight or weight in relation to skeletal chest-frame diameter as seen in chest X-ray films.

Measurements of the fat-plus-skin thickness at the level of the 10th rib was also used by the investigators as a more direct method of determining obesity. The fatty layers were seen as shadows on the X-ray films and ranged in thickness from 2 to 15 millimeters, averaging 7.4 millimeters thick.

Serum cholesterol values varied in the students from 140 to 386 milligrams per 100 milliliters of serum and averaged 225 milligrams per 100 milliliters.

The study revealed an insignificant correlation ("not significantly different from zero at the 5-percent level of confidence") between serum cholesterol levels and direct and indirect obesity measurements.

"The lack of relationship between the amount of body fat and the serum cholesterol level demonstrated in the present study supports the view that the nutritional status of healthy young men such as medical students is considerably less important in determining the cholesterol level than other biologic factors," conclude the investigators.

Several of these biologic factors, which include age, sex, race, heredity, endoctrine patterns, habits of smoking and exercise, and emotional stress, have been previously reported by Dr. Thomas and coworkers to bear a positive relationship to high serum cholesterol levels among the Johns Hopkins medical students.

Find mucopolysaccharides not causally related to atherosclerotic lesions

Because mucopolysaccharides are often found in increased amounts at the site of atherosclerotic lesions, they have been suspected of being a causative factor in atheroma development. However, studies of the aortas of cholesterol-fed rabbits suggest that the increased amounts of mucopolysaccharides usually found in arterial tissue at the site of atherosclerotic lesions are secondary to fat deposition rather than a cause of it. The studies, supported in part by an NHI grant, were carried out by Drs. A. J. Bollet, Wayne State University College of Medicine, Detroit; Chuni Wang, Detroit Receiving Hospital; and David Adlersberg, Mount Sinai Hospital, New York. Their findings are reported in Circulation Research (8: 88–92).

Mucopolysaccharides are found in the connective tissues which bind together and support the cellular components of blood vessels and many other organs. The supportive function is accomplished by the protein collagen, whose insoluble fibers are embedded in a soluble matrix called the ground substance. Mucopolysaccharides are important constituents of the ground substance.

In recent years studies on the possible role of the arterial ground substance in atherosclerosis have shown that the development of atherosclerotic lesions appears to be accompanied by increased concentrations of mucopolysaccharides in the affected tissues. Animal studies also showed that cortisone (which retards mucopolysaccharide metabolism) slowed the development of atherosclerotic lesions while the enzyme hyaluronidase (which breaks down the mucopolysaccharide hyaluronic acid) counteracted the effects of cortisone. These findings suggested that changes in mucopolysaccharides are important in atheroma formation and might even be a causative factor.

To investigate this possibility, the scientists induced atherosclerosis in rabbits by feeding them cholesterol for 1 to 7 months. Animals were sacrificed at 2-week intervals after the first month and their aortas analyzed both for lipids and for mucopolysaccharides. Early atherosclerotic changes were found in the aortas of animals after 1 to 2 months of cholesterol feeding, and moderate to severe lesions in animals fed cholesterol for 3 months or more. However, chemical analysis of the mucopolysaccharide content of these vessels showed no significant increases except in the more advanced lesions produced by 6 months or more of cholesterol feeding.

The findings suggest that alterations in mucopolysaccharides are indeed related to lipid changes in the development of atherosclerotic lesions, but are secondary to lipid deposition, not a cause of it.

NHI findings support filtration theory of atherosclerosis

Evidence supporting the filtration theory of atherosclerosis has been obtained from studies on experimental atherosclerosis conducted by Dr. Leroy Duncan, Mrs. Katherin Buck, and Mr. Almorris Lynch, of the NHI Laboratory of General Medicine and Experimental Therapeutics.

The filtration theory assigns the chief role in the development of atherosclerosis to lipoproteins, fat-protein complexes which serve as the major vehicles of lipid transport in the body. According to this theory, intact lipoproteins carrying cholesterol pass from the plasma into the inner layer of the arterial wall. Here, because of the structure of the wall, they are trapped and give rise to atheromatous lesions.

The studies on experimental atherosclerosis were based on information gained in previous studies on the movement of plasma albumin into arterial walls. These studies had disclosed that albumin enters the aorta with a gradient of rates, entering most rapidly in the upper aorta and progressively more slowly down its length. The investigators reasoned that plasma albumin and plasma lipoprotein might enter aortic wall by the same mechanism and thus show the same gradient of rates. When combined with the filtration theory, this reasoning led to the prediction that there should also be a gradient in the deposition of cholesterol along the length of the aorta early in the development of experimental atherosclerosis.

Subsequent determinations of the cholesterol concentrations along the length of aortas in dogs confirmed the prediction. Early in experimental atherosclerosis there is a striking gradient of cholesterol deposition, and this gradient is very similar to the gradient of rates with which albumin enters the aortic wall. The experimental demonstration of this consequence of the filtration theory offers strong support for that theory.

The scientists found that the gradient disappears later in the development of experimental atherosclerosis, and that the cholesterol concentrations eventually become higher in the lower portion of the aorta. This sequence of events suggests that the most severe atheromatous lesions tend to localize eventually in the lower aorta because of the extremely slow removal of cholesterol from that segment.

These studies, reported in Circulation Research (8: 1023–27), also emphasize that the interplay of the rates of deposition and removal of cholesterol from the arterial wall are of prime importance in the development of atherosclerosis. Studies on factors influencing these rates are in progress.

Blood Pressure

New hypotensive drugs minimize side effects by selective action

Syrosingopine and guanethidine, two new hypotensive drugs, synthesized and marketed by Ciba, have been found to be effective in lowering blood pressure and also specific enough in their modes of action to minimize undesirable side effects. Scientists of the NHI Laboratory of Chemical Pharmacology have found that both drugs lower blood pressure by depleting the peripheral sympathetic nerve endings of norepinephrine, thereby blocking the transmission of nerve impulses that trigger blood vessels constriction.

Drugs that lower blood pressure by peripheral sympathetic blockade are not new; some have been in use for years. Most of these work by inhibiting the action of norepinephrine, an amine that is released from sympathetic nerve terminals to transmit their impulses to the muscles of the arterial wall. Reserpine was the first drug found to lower blood pressure by depleting this amine at sympathetic terminals; but only slightly larger doses may also produce undesired sedation and parasympathetic effects by depleting brain amines, and diarrhea by releasing serotonin in the intestines. A major problem in treating hypertensives with reserpine has been the maintenance of dosage schedules that would hold blood pressure down without causing these side effects.

Syrosingopine, a compound made by "tailoring" the reserpine molecule slightly, resembles reserpine in its effective effects on blood pressure, but is more selective in its site of action. In experiments on animals, Drs. Barbara H. Orlans, Kenneth F. Finger, and Bernard B. Brodie compared the effects of reserpine and syrosingopine on peripheral norepinephrine and on brain amine levels. Both drugs depleted peripheral norepinephrine in doses that did not affect brain amines: however, reserpine exhibited this selectivity only over a narrow dosage range, whereas syrosingopine did not affect brain amines over a wide range. This more selective peripheral action of syrosingopine is a highly desirable clinical feature that provides a greater margin of safety against undesirable side effects.

Guanethidine, a synthetic drug structurally different from reserpine, is also far more specific in its action than is reserpine. The drug depletes the peripheral sympathetic nerves of norepinephrine, but does not affect brain amine levels (due in part to its limited ability to penetrate the blood-brain barrier), therefore does not produce sedation. It does not release serotonin from peripheral body tissues, thus does not cause diarrhea. The drug is also well suited to oral administration because it is stable in the gut and is more readily absorbed than are ganglionic blocking agents.

The work by Drs. Rosemary Cass, Ronald Kuntzman, and Bernard B. Brodie did not disclose the precise mechanism by which guanethidine depletes peripheral norepinephrine, even though the results indicate that it does so by a mechanism different from that of reserpine. There are two possibilities, both under study: the drug may impair storage of the amine or block its synthesis.

The findings on the two drugs are reported, respectively, in the Journal of Pharmacology and Experimental Therapeutics (128: 131–139) and in Proceedings of the Society for Experimental Biology and Medicine (103: 871–872).

Neurological disturbances in catron-treated patients due to common amino acid

Tryptophan is an essential amino acid found in many dietary staples, and which, under normal circumstances, produces no untoward effects on the consumer. However, when given to patients receiving monoamine oxidase (MAO) inhibitors, tryptophan is capable of producing pronounced neurological disturbances, some of them strikingly similar to those of alcoholic intoxication.

These disturbances were observed by Drs. John A. Oates and Albert Sjoerdsma, of the NHI Laboratory of General Medicine and Experimental Therapeutics, after giving tryptophan orally to seven hypertensive patients being treated with catron, a potent MAO inhibitor. The doses of tryptophan producing these effects were only 1½ to 3 times the usual dietary intake of this amino acid. This small difference raises the question of whether diets unusually high in this or other amino acids might not modify the clinical effects and side effects of MAO inhibitors in the treatment of hypertension and especially in the treatment of certain depressed states.

In three of these patients, tryptophan produced irregularities of coordination, euphoria, release of inhibitions, slurred speech, and other effects strikingly similar to those of alcoholic intoxication. These and other patients also showed signs of drowsiness, a sharp contrast to the psychic energizing effects usually produced by NAO inhibitors. Four patients receiving the largest doses of tryptophan also exhibited exaggerated reflexes, confined chiefly to the lower extremities, and accompanied by spasms of the ankle.

The fact that tryptophan produced these effects only in patients receiving MAO inhibitors suggests that the effects might be due to one or more of the amines produced from this amino acid. The most likely suspects are tryptamine and serotonin.

Animal studies have shown that doses of tryptophan increase the levels of both of these amines in the brain, and that this increase is augmented by MAO inhibitors. These inhibit the destruction of tryptamine and serotonin by the enzyme monoamine oxidase at the same time that tryptophan is leading to stepped-up amine production. Increased levels of either or both amines are accompanied by neurological effects that vary according to the species of animal.

In man the evidence is less direct, but tryptophan has been shown to increase urinary excretion of tryptamine and an end product of serotonin metabolism 5-hydroxyindole acetic acid (5–HIAA). Thus it is reasonable to assume that levels of both amines in the nervous system are increased by tryptophan and MAO inhibitors, and that either or both amines may be responsible for the observed neurological effects.

These findings have been accepted for publication in Neurology.

Chronic renal hypertension not dependent on pressor substances from kidney

Animal studies on the role of the kidney in hypertension have provided evidence that the chronic elevation of blood pressure that persists in renal hypertension is not dependent on increased blood levels of artery-constricting substances from the kidney. The studies, supported in part by an NHI grant, are reported in the American Journal of Physiology (198: 1148–1152) by Drs. Pedro Blaquier, David F. Bohr, and Sibley W. Hoobler, of the University of Michigan.

The kidney is known to be the villain in several forms of secondary hypertension and has also been suspected of playing a role in the development and/or maintenance of essential hypertension. It has been demonstrated that the kidney releases renin as an acute response to an inadequate renal blood supply; and that renin, in turn, reacts with a serum protein to form angiotensin, a potent artery constrictor. But whether this response is transient or is involved in the maintenance of chronic hypertension has been the subject of much conflicting evidence.

In the study of this problem, the scientists used a cross-circulation technique in which the femoral arteries and veins of rats with surgically produced renal hypertension were connected by plastic tubing to those of normotensive rats. Preliminary work had shown that (1) cross circulation between pairs of normotensive rats produced no significant changes in blood pressure, and (2) elevated blood pressure produced in one of the pair by infusions of renin or angiotensin was followed shortly by elevated blood pressure in the other. Thus, if the hypertension in the surgically treated rat were due to circulating vasoconstrictors, cross circulation should also produce hypertension in the normotensive rat of each pair.

To rule out blood pressure aberrations that might be due to blood volume changes, normal and stable blood volumes were maintained by equalizing the flow rates between the animals of each pair by adjustable clamps on the plastic tubing. The animals were arranged on the two pans of a sensitive balance so that any volume variations would be promptly noted and corrected.

In one series of experiments the scientists used seven rates whose renal arteries had previously been clamped for 4 hours. When the clamps were removed, hypertension was produced within minutes, presumably by renin from the ischemic kidney. Cross circulation, immediately initiated between these rats and seven normotensives, resulted in elevated blood pressure in all normotensive rats. However, cross circulation between normotensive rats and those with hypertension of more than 1 week's duration had no significant effect on the blood pressure of the normotensives.

Thus, it appears from these experiments that circulating artery-constricting substances such as renin may play some role in the initiation of renal hypertension, but may not contribute to its maintenance.

Diet-induced hypertension in rats similar to human essential hypertension

Studies on rats made hypertensive by diets deficient in potassium or choline during early life suggest that this dietary technique may yield laboratory animals more suitable for research on the role of the kidney in essential hypertension than do commonly used methods involving renal artery constriction or removal of one kidney. Renal function studies on rats showed that the diet-induced hypertension in these animals, like essential hypertension in humans, was not the result of an inadequate renal blood supply nor was it associated with severe excretory insufficiency.

In these experiments, Drs. Fred N. White, M. P. Sambi, and Arthur Grollman, of the University of Texas Southwestern Medical Center, studied renal function in 31 rats: 10 normal controls and 21 with diet-induced chronic hypertension. The NHI grantees compared data from the two groups to determine the effects of the experimental hypertension on rates of renal blood flow, plasma filtration by the kidney glomeruli, and excretion of urea.

Their findings, reported in the American Journal of Physiology (198 (2), 221–222, 1960), revealed significant changes from normal only in the glomerular filtration rates, which were somewhat reduced in the hypertensive rats. The findings suggest certain striking similarities, with respect to renal function, between diet-induced experimental hypertension and the essential hypertension that develops spontaneously in humans. Neither is the primary result of an inadequate renal blood supply and neither is accompanied by severe impairment of excretory capacity.

These similarities suggest that the dietary technique might yield laboratory animals especially suitable for research on kidney function and hemodynamics in hypertension, especially on more subtle renal changes that might be masked by the severe lesions and renal ischemia usually resulting from drastic surgical procedures. Furthermore the dietary procedure is simpler and less subject to failure than are most surgical techniques. The potassium or choline deficient diets need to be fed to the animals for only a short period (usually 1-5 weeks) early in their lives to produce hypertension, after which the disease is self-maintaining and progressive.

Previous studies by Drs. Grollman and White, who developed the technique, indicate that the morphological changes induced in the heart, blood vessels, and kidneys by diet-induced hypertension are also similar to those of essential hypertension in humans. Thus the technique may aid in the accumulation of experimental data that might establish relationships between experimental hypertension in animals and essential hypertension in man. Such relationships might help to clarify many of the puzzling features of this enigmatic disease.

SURGERY

Cardiac shunts detected by heart injections of Krypton-85

Studies by NHI scientists on 48 patients have shown that radioactive krypton, injected directly into the heart via a cardiac catheter, provides a simple, rapid, and accurate means of detecting and localizing cardiac shunts. The small quantities of the isotope needed for the procedure and its short biological half-life make the method safe both for the patient and for laboratory personnel.

Shunts result from holes in the partition separating the right heart from the left heart. The right heart receives oxygen-poor blood from the body and pumps it to the lungs; the left heart receives the freshly oxygenated blood from the lungs and pumps it to the body. By allowing the mixing of oxygen-poor blood with oxygenated blood in the heart, shunts can seriously impair the efficiency of the heart in delivering oxygen to the tissues.

To detect left-to-right shunts, a catheter is positioned in the left heart and 3 to 5 milliliter of saline containing dissolved krypton-85 injected. If no shunt exists, the gas will be pumped throughout the system and largely dissipated before making a much delayed appearance in the lungs via the right heart. But a left-to-right shunt will allow some of the gas to cross to the right heart, where it is pumped directly to the lungs. Thus, shortly after the injection the gas will appear in high concentration in the air exhaled by the patient. The radiation of the expired air is monitored by a count-rate meter and recorded continuously on a direct-writing oscillograph.

To detect right-to-left shunts, the krypton-85 is injected into the right heart and arterial blood samples drawn at a constant rate for the next 15 seconds. In the absence of a shunt, all of the gas is pumped to the lungs where about 95 percent of it is eliminated in the expired air before entering the arterial circulation. Thus high concentrations of the isotope in the arterial samples mean that the gas bypassed the lungs by crossing directly to the left heart.

Repeated injections of krypton 85 with the catheter tip stationed at different points makes it possible to localize shunts with a considerable degree of accuracy. The method also permits estimation of the magnitude of right-to-left shunts by relatively simple calculations.

In every patient in which this technique indicated the presence or absence of a shunt, its accuracy was subsequently verified by findings at operation or autopsy, or by the use of other established techniques for diagnosing shunts. These included selective angiography, dye dilution curves, and krypton 85 or nitrous oxide inhalation tests. The method proved to be convenient, simple to apply during heart catheterization, and sensitive enough to permit the detection and localization of even very small shunts.

These clinical studies were conducted by Drs. R. T. L. Long, Eugene Braunwald, and A. G. Morrow, of the NHI Surgery Branch. Their findings are reported in Circulation (8: 1126–1133).

Superiority of butanol cardioplegia revealed by animal studies

The frequently observed depression of heart action in patients following elective cardiac arrest has stimulated the quest for better methods of stilling the heart. Chemical methods (aortic injections of potassium citrate or acetylcholine) have been largely abandoned in favor of the anoxic method which involves clamping the aorta to restrict bloodflow to the heart. Now evidence that butanol-induced cardioplegia has certain advantages over the anoxic method is reported in the Transactions of the American Society for Artificial Internal Organs (6: 323–337) by Drs. H. H. McGuire, Jr., L. H. Bosher, Jr., and R. W. Ramsey, of the Medical College of Virginia, Richmond. Their studies were supported by a National Heart Institute grant.

The scientists divided 21 dogs into 4 groups according to type and duration of cardioplegia : butanol arrest of 15 or 30 minutes duration, and 15 or 30 minutes anoxic arrest. Control ventricular function data was obtained for each group prior to arrest for comparison with similar data obtained 15 and 30 minutes after cessation of arrest.

Comparison of the postarrest ventricular function curves showed that recovery following 15-minute arrest was much more rapid in the butanol-treated animals than in the anoxic arrest group. At 15 minutes postarrest, for example, ventricular function had returned to 85 percent of normal in the butanol-arrested animals, but to only 49 percent of normal in the others. Recovery after 30-minute butanol arrest was less satisfactory, but was still much more rapid than that after 30-minute anoxic arrest.

Although the protection conferred by butanol appears to diminish if cardioplegia is maintained for longer than 15 minutes, the scientists feel that this protection might be extended for longer periods by the use of hypothermia or auxiliary metabolic or cardioplegic agents.

New catheter design permits selective visualization of coronary arteries

A new coronary arteriography procedure, involving the use of a special loop-end catheter, is reported in the New England Journal of Medicine (262: 325–333) by NHI grant-aided scientists in Boston. Their studies in dogs and humans show that the technique permits safe, selective X-ray visualization of the coronaries with smaller amounts of radiopaque dye than is usually required by other procerures. Further application of this technique may improve X-ray diagnosis of coronary artery disease.

The Boston scientists are: Drs. Sven Bellman, H. A. Frank, P. B. Lambert, David Littmann, J. H. Hall, and J. A. Williams of Beth Israel Hospital, West Roxbury Veterans' Administration Hospital, and Harvard Medical School.

In coronary arteriography, a radiopaque substance is injected through a catheter into the base of the aorta where the coronary arteries branch out into the heart. As contrast substance flows into the coronaries, rapid-sequence X-ray pictures are taken to reveal the extent and location of atherosclerotic deposits. Success of the procedure depends upon an adequate flow of contrast medium into the coronaries, and has been accomplished in the past by either injecting large quantities of medium or by diverting more contrast material into the coronaries through aortic occlusion or temporary heart arrest. While usually safe and reliable, adverse reactions have been observed in some patients receiving large dye injections.

The new technique employs a different principle of injection whereby dye is injected through holes in the catheter-loop and directed toward the coronary openings, thus eliminating the necessity for large amounts of dye. The loop-end catheter was developed by the scientists after their dog studies had shown that ordinary, straight-tipped catheters recoil away from the coronary openings as dye is injected.

The catheter-loop is held straight by a wire guide while being inserted into the aorta and regains its circular shape upon withdrawal of the guide. The synchronous injection of dye and rapid-sequence exposure of X-ray plates may be repeated for a second set of films.

The Boston workers report that coronary arteriography with the loop-end catheter was well tolerated by both dogs and humans, and that good coronary visualization was regularly obtained. They expressed the belief that this method is inherently safer than other methods currently available, and concluded, "This approach to the problems of angiographic diagnosis of coronary artery disease shows considerable promise."

The loop-end catheter method is one of several recent developments in coronary arteriography and illustrates progress being made in this field.

Technique increases safety of surgery to unblock small arteries

A new technique that permits surgical removal of atherosclerotic deposits, clots, or other lesions obstructing blood flow in small arteries has been developed by Drs. E. S. Crawford, A. C. Beall, P. R. Ellis, Jr., and M. E. DeBakey of the Baylor University College of Medicine. The new method overcomes the problem formerly posed by the constriction of the inner diameter of the artery at the site of the incision during the healing process. This is done by inserting a knitted dacron patch at the incision site (following removal of the arterial obstruction), then suturing the wound edges to this patch rather than to one another.

After being tested on laboratory animals, the technique was used in 93 patients suffering from lesions impeding arterial blood flow. At the site of arterial blockade a longitudinal incision was made through the artery wall, cutting through all of the diseased portion plus a short undiseased arterial segment at either end. A piece of plastic tubing was inserted to detour blood around the site while the obstruction was removed. The dacron patch was then inserted and the wound edges sutured to its circumference, the plastic tubing detour being withdrawn just before the final suture was drawn taut.

None of these patients developed recurrent arterial obstruction during their convalescence, and only two had recurrences during the next 30 months. This is in sharp contrast to the results of animal studies in which incisions, made in arteries of comparable diameter, were repaired by suturing the wound edges together. Every artery repaired in this way subsequently became constricted.

Endarterectomy, the direct surgical removal of lesions obstructing blood flow, has been used successfully to restore normal circulation in such large arteries as the aorta and iliac. Theoretically, the same technique should be even better suited for obstructed small arteries, such as the coronary, renal, or vertebral arteries, since lesions tend to be confined to short segments of such vessels. However, its application had previously been sharply limited by the constriction that often developed in such vessels after surgical repair—a factor of great importance in small vessels because of the attendant danger of clot formation.

By overcoming this problem, the new technique greatly extends the use of surgery for the correction or improvement of arterial insufficiency resulting from atherosclerosis or other cardiovascular diseases. It may also make possible the safe and effective use of surgery in the treatment of coronary heart disease, heretofore attended by high risk and low probability of success.

This work, which was supported in part by an NHI grant, is reported in Surgical Forum (10: 671–675).

Combat heart arrest by massage through unopened chest

A new method of closed-chest cardiac message which may be used by "anyone, anywhere" to restore blood flow in patients with cardiac arrest, is described in The Journal of the American Medical Association (173: 1064–1067) by Drs. W. B. Kouwenhoven, J. R. Jude, and Mr. G. G. Knickerbocker of the Johns Hopkins University School of Medicine at Baltimore. The method, which they developed through extensive experimentation on more than 100 dogs, has been used with notable success on patients with cardiac arrest.

The new technique is easily applied and, unlike direct cardiac massage, it eliminates the necessity for surgical exposure of the heart. To effect massage, the operator places both hands, one above the other, with the heel of the lower hand resting on the lower third of the patient's sternum and presses vertically downward about 60 times per minute. With each pressure stroke the sterum is moved 3 or 4 centimeters toward the spine, thus compressing the heart and forcing out blood. Relaxation at the end of the stroke allows the heart to fill again. Artificial respiration should be given simultaneously.

"When cardiac arrest occurs," the scientists point out, "the circulation must be restored promptly; otherwise anoxia will result in irreversible damage." They found that closed-chest cardiac massage, combined with artificial respiration, maintains a flow of oxygenated blood to the heart and central nervous system until normal heart action returns spontaneously or, in cases of ventricular fibrillation, until a closed-chest defibrillator can be brought to the scene of the emergency. According to the investigators' experience, hearts in fibrillation for longer than 3 minutes usually do not respond to defibrillation procedures. Closed-chest cardiac massage, however, greatly extended this time limit: "Adequate circulation for periods as long as 30 minutes was easily maintained with the dog in ventricular fibrillation. A closed-chest defibrillating shock would result in the immediate return of normal sinus rhythm in such animals," they explain.

In the 10 months preceding their report, Dr. Kouwenhoven and coworkers applied closed-chest cardiac massage to 20 patients who were from 2 months to 80 years of age. In addition to cardiac massage, which varied from less than 1 minute to 65 minutes in duration, 3 patients required defibrillation and 13 required artificial respiration. The scientists report that all 20 patients were successfully resuscitated and, at the time of this report, 14 patients were alive without central nervous system damage; an overall permanent survival rate of 70 percent.

Although their data was obtained from hospitalized patients, Dr. Kouwenhoven and coworkers conclude, "The real value of the method lies in the fact that it can be used wherever the emergency arises, whether that is in or out of the hospital."

Portable pacemaker aids patients with complete heart block

Electrical stimulation of the heart with a transistorized portable pacemaker is reported to be an effective method of treating complete heart block in patients. A description of the apparatus and its use in 66 patients is reported in the Journal of the American Medical Association (172: 2006–2010) by Drs. C. W. Lillehei, V. L. Gott, P. C. Hodges, Jr., D. M. Long, and Mr. E. E. Bakken of the University of Minnesota Medical School at Minneapolis.

In complete heart block, disease or operative injury of the heart's conduction tissue blocks nerve impulse conduction from the sinoatrial node (the heart's "pacemaker" located in the right atrium) to the ventricles. The ventricles thus lose their normal rhythm and frequently cease beating entirely.

The artificial pacemaker developed by the Minnesota workers is designed to maintain the heartbeat for days, weeks, or even months—until diseased or injured tissue regenerates and the heart's own pacemaker can resume maintenance of normal heart rhythm. The device consists of a transistorized transformer powered by a self-contained long-life battery, and is connected to the heart by one or two thin wire electrodes inserted into the heart muscle.

Electrode(s) may be inserted either through the open chest or, in nonsurgical patients, by piercing the chest wall with a hollow needle, through which an electrode is passed and the needle subsequently withdrawn. The small pacemaker (slightly larger than a package of cigarettes) is completely portable and is worn strapped to the patient's chest.

The NHI grant-aided scientists report that artificial pacemaker stimulation has proved to be the most effective method of managing complete heart block in surgical patients, and that two-thirds to three-fourths of these patients required less than 2 or 3 weeks of continuous stimulation. Most of the remaining surgical patients were "weaned" from the pacemaker by progressively lowering the rate of stimulation and administering isoproterenol hydrochloride, a drug which increases cardiac rhythmicity and rate.

Most of the patients treated in this series had developed heart block subsequent to cardiac surgery. However, the pacemaker has also been used successfully in the treatment of Stokes-Adams syndrome—heart block due to atherosclerosis, infection, or certain drugs—restoring many of its victims to useful activity. The investigators point out that, not only has the threat of sudden death in these patients been removed, but that their physical and emoional rehabilitation has been dramatic. At the time of their report, one patient with Stokes-Adams syndrome had been maintained under continuous stimulation for 15 months.

New aortic valve prostheses reported by NHI grantees

University of Minnesota surgeons David L. Long, Jr., Laurence P. Sterns, Robert H. De Reimer, Herbert E. Warden, and C. Walton Lillehei, described in Surgical Forum (10: 660–665) two different types of plastic valves which they developed for the replacement of irreparably damaged aortic valves. They report that one type of valve has been used with success in patients.

Both valves—a flap valve and a bicuspid valve—are constructed of silastic (a rubbery silicone plastic) bonded to a polyvinyl sponge (Ivalon) base. They are inserted through a slit in the aorta and secured by sutures at the site of the natural aortic valve.

Both valves have been tried in dogs. They were also tested in human cadaver hearts which were made to "beat" in a mechanical pulse duplicating apparatus.

Flap valves were successfully inserted by the Minnesota surgeons in two patients, with subsequent restoration of valvular function in each case. The investigators report that the first patient was well and active at the time of their report, 11 months after surgery, and that he second patient was well and active following the operation but died 2 months later of an unrelated cause. Autopsy revealed a properly positioned, functional valve with no abnormal blood clots present.

Function and durability tests of the bicuspid valve in a pulse-duplicating machine have been very encouraging, but complications that occurred upon installation of the valve in dogs delayed clinical trials. Difficulties encountered included leakage of blood between the valve and aortic wall in some animals before a suitable method was devised for securing the valve. Complete heart block also developed in some animals as a result of damage to heart-impulse-conduction tissue by sutures or internal bleeding. The investigators believe that in the human heart the larger size of the structures may make it possible to avoid this complication.

Results of the Minnesota studies suggest, conclude the investigators, "that substantial progress has been achieved in the resolution of many of the very significant problems concerned in the use of artificial cardiac valves. Moreover, this same progress, culminating in successful clinical application, has served to point the way for numerous further improvements in choice of materials, design, and surgical technique."

Artificial heart prototypes designed and tested by NHI grantees

The design and preliminary trials of two prosthetic hearts are reported in the American Heart Journal (59: 723–736) by Drs. C. S. Houston, Tetsuzo Akutsu, and W. J. Kolff at the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute in Cleveland. Studies of the mechanical hearts in dogs and in a mock circulatory system indicate that progress is being made toward replacing irreparably damaged human hearts with mechanical pumps implanted within the chest. These pumps, however, are not sufficiently developed to warrant their installation in humans.

Each of the new prostheses—a pendulum-type pump and a roller-type pump—contains an electric motor and two elastic pumping chambers, or ventricles, of polyurethane plastic. Polyurethane valves and connecting tubes maintain unidirectional blood flow through the hearts, and plastic-coated wires supply current from an externally located battery pack or wall socket to power the hearts.

In the pendulum pump, a motor suspended on pivots (the "pendulum") swings back and forth within a rigid outer housing, alternately compressing each ventricle against the housing. To-and-fro excursions of the motor pendulum are caused by an eccentrically mounted, adjustable lever arm which connects the motor shaft with the outer housing.

Tests of the pendulum pump in a mock circulatory system showed that as much as 1,800 milliliters of blood per minute is ejected from each ventricle and that hemolysis of red blood cells by the pump is not excessive, report the Cleveland scientists.

Encouraged by these tests, they installed a pendulum pump at the anatomical site of the natural heart in a 30-kilogram dog, which was maintained by a heart-lung machine during removal of its own heart. The investigators report that the dog's circulation was sustained for 5 hours by the pump, but that several infusions of norepinephrine were required to maintain blood pressure. The pump had been adjusted to deliver 2,000 milliliters per minute which, they explain, was inadequate for a dog of this size. The pendulum pump, however, "seemed promising enough to serve as a model for a more durable pump, which is under construction," they report.

The second type of pump designed by the Cleveland group employs a small, motor-driven roller to compress the ventricles against a rigid outer housing. Polyurethane foam inserted between the ventricles and housing provides a yielding surface which minimizes hemolysis.

In mock circulation tests of this pump, ventricular outputs increased (in the left ventricle, from 200 to 2,200 milliliters per minute) as atrial pressures were increased. Thus, the output on both sides are self-regulating; if one side pumps more blood than the other, the increased atrial pressure on the other side leads to an increased output by that side.

In a single animal experiment, the roller pump sustained a dog for 2 hours. Although the pump was not sufficiently streamlined to allow closure of the dog's chest, there was evidence of spontaneous breathing and of excellent blood oxygenation; pressure tracings indicated good functioning of the pump.

NEW KNOWLEDGE AND METHODS

New diuretic is effective against edema or normal or toxemic pregnancy

Hydrochlorothiazide, a new diuretic drug derived from chlorothiazide, has been found highly effective against the edema of normal or toxemic pregnancy.

In NHI grant-supported studies at the University of California Medical Center, Dr. N. S. Assali used hydrochlorothiazide, as Esidrex (Ciba) and HydroDiuril (Merck, Sharp & Dohme), to treat 33 patients with edema accompanying normal pregnancy and 25 edematous patients with toxemia of pregnancy. His findings, reported in Clinical Pharmacology and Therapeutics (I, 48–52), indicate that the diuretic action of the new drug closely resembles that of chlorothiazide, but appears to be effective at one-tenth the dose.

Edema is the accumulation of fluid in the extracellular tissue spaces. Its most common cause in normal pregnancy is too much salt in the diet or salt retention by the kidneys. Edema in toxemia of pregnancy is also associated with salt retention, and may be abetted by the loss of protein in the urine that also characterizes this disorder. Although slight or moderate edema is more unsightly than clinically dangerous, severe edema can lead to fluid accumulation in the abdominal cavity (ascites) or in the chest, where it can seriously interfere with respiration.

Like chlorothiazide, hydrochlorothiazide reduced edema by increasing renal excretion of salt, potassium, and water; but 100 to 150 milligrams seem to produce effects comparable to those produced by 1,000 to 1,500 milligrams of chlorothiazide in a previous study. The drug appears to increase salt and water excretion by inhibiting their reabsorption in the kidney tubules, since it produced no significant effects on renal plasma flow or filtration rates.

The drug produced no observed adverse effects, did not noticeably alter serum electrolyte levels in most patients, and produced most marked diuresis in patients whose edema was most severe. As edema diminished, the effects of the drug were reduced. This is a very desirable feature of the drug because it provides a margin of safety to protect against the possibly serious consequences of electrolyte depletion.

Developments extend use of gas chromatography in lipid analysis

Important new contributions by NHI scientists have made possible the use of gas chromatography for the radioassay of fatty acids labeled with radioactive carbon and for the analysis of steroids. These developments should greatly facilitate research on lipids and lipid metabolism and the possible roles of these factors in atherosclerosis.

Originally developed in England in 1952, gas chromatography has helped solve many problems of lipid analysis formerly posed by analytical methods that were complex, slow, and insufficiently accurate for the assay of small samples. In gas chromatography, a small sample of the lipid mixture to be analyzed is injected into an analytical column, vaporized, and swept through the column on a stream of inert carrier gas (argon or helium).

In transit through the column the lipid vapors are brought into repeated contact with a nonvolatile liquid, present as a thin coating either on the inner surface of the column or on small inert particles with which the column is packed. All of the lipids are soluble in this liquid, but the extent varies with their structure and chemical properties. This variation affords the means of separating the lipid components (the more soluble the lipid, the slower its transit and vice versa) and also for identifying each component as it emerges. As it emerges from the column the lipid vapor enters a special detector which senses its passage, measures its concentration, and records these data against time on a strip chart.

The system for the radioassay of carbon-14 labeled fatty acids by gas chromatography was worked out by Drs. Arthur Karmen and Harold R. Tritch, of the Laboratory of Technical Development. The system, described in Nature (186: 150–151), uses a short column containing anthracene crystals coated with silicone oil to trap the fatty-acid vapors emerging from the analytical column.

The radioactive vapor dissolves in this oil, thereby coming in close proximity to the anthracene crystals. The radiation emitted causes small flashes (scintillations) in the crystals. These scintillations are detected by phototubes and counted by an automatic scintillation counter.

The system allows the collection of individual fatty acid esters in separate trapping columns or for continuous monitoring of a single column. In the latter method, a device measures the rate at which scintillations are occurring and plots this against time on a strip chart. As each new component enters the trapping column, this rate increases sharply. From this data can be determined the time that each component entered the column and how much radioactivity it contained.

The use of gas chromatography for the analysis of steroids was made possible by a special analytical column designed by Drs. W. J. A. VandenHeuvel, C. C. Sweeley, and E. C. Horning, of the NHI Laboratory of the Chemistry of Natural Products.

Steroids, the subject of intense scientific study in recent years, are members of a large family of compounds which include cholesterol, many important adrenal hormones, several vitamins, and the male and female sex hormones. Previous attempts had been made to separate and analyze steroids by gas chromatography, but had been at best only partly successful. Unfortunately, with ordinary liquid phases and column temperatures, most steroids were so soluble in the liquid phase that they would be retained too long in the column. As a result, many heat-sensitive steroids would decompose before entering the detector.

The scientists overcame these problems with a column whose inert particles were coated with a very thin film of methyl silicone gum. The column could be used at low temperatures and gave rapid transit times, a combination which solved the steroid heat-sensitivity problem. At the same time it provided high sensitivity—being able to analyze samples weighing as little as one millionth of a gram—and could separate components differing only very slightly in their molecular structure.

In addition to offering a unique combination of speed, sensitivity, and high resolution, the column has proved to be versatile as well. It has been used successfully to separate and analyze a large number of alkaloids, an enormous family of plant substances which has yielded many valuable drugs over the years.

The column and its uses were reported at the Milan Symposium on Drugs Affecting Lipid Metabolism and in the Journal of the American Chemical Society (82: 3481, 3791).

Report gas chromatography detector based on sound velocity variations

An engineer in the NHI Laboratory of Technical Development has designed detecting equipment utilizing measurement of sound velocity in gases for characterizing the constituents of samples separated by gas chromatography.

For maximum usefulness as an anlytical tool in the biologic sciences, the principle of gas chromatography as introduced from England has required the design and incorporation of more sensitive and versatile systems for detecting the constituents of complex samples once the chromatograph had separated them.

Investigators in the NHI Laboratory of Technical Development have attacked this problem on several fronts with notable success, designing and developing detecting systems which permit extension of gas chromatography to many new research areas.

New detecting equipment using variations of measured sound velocity was described by Frank W. Noble at the 13th Annual Conference on Electrical Techniques in Medicine and Biology held in Washington, D.C. The velocity of sound passing through a gas varies according to the physical properties of the gas, such as its molecular weight. With the equipment described, voltage is applied to a sound-transmitting crystal at one end of a tube containing the sample, and recorded by a receiving crystal at the other end. Phase differences induced by particular samples, between the two voltages are sufficiently definitive to imply analytical usefulness for the principle.

The actual value of the sound velocity principle as used in the equipment Mr. Noble described remains to be demonstrated in applied research.

Drug metabolism by liver unaltered in patients with cirrhosis

Preliminary studies at NHI and New York University suggest that normal rates of drug metabolism are not altered by cirrhosis, despite severe loss of functioning liver, wherein are located the special enzyme systems that inactivate drugs. Thus, the presumed sensitivity to certain drugs of patients with liver disease may require some other explanation, if these indications are borne out by more extended studies.

Conversion of certain fat soluble foreign compounds, such as drugs, into inactive derivatives is an important function of the liver, without which the action of many drugs would persist for a dangerously long time. The liver disposes of such compounds by converting them to derivatives which are less fat soluble, thus barring them from reabsorption into the body through the fat-like membrane lining the kidney tubules.

Recently Dr. Bernard B. Brodie and Dr. John Burns of NHI, and Dr. Murray Weiner of New York University Research Service compared the inactivation of various drugs in patients with severe Laennec's cirrhosis and in normal subjects. The drugs studied (phenylbutazone, aminopyrine, antipyrine, salicylic acid, and dicumarol) had previously been shown to be metabolized in the body through the action of liver enzymes.

The biologic half-life of these drugs was not significantly different in the cirrhotics and controls, indicating that the activity of the enzyme systems involved was not appreciably affected by the liver-damaging disease. Special precautions are usually advised in the administration of certain other drugs to patients with liver disease, for it is commonly believed that drug metabolism is generally impaired in the diseased liver. The present studies should be extended to patients with other types of liver disease as well as to other compounds that are metabolized along similar other pathways. If indications of the present findings are borne out by further study, some other explanation should be sought for the presumed sensitivity to certain drugs of patients with impaired liver function.

These findings were published in Medicina Experimentalis (1: 290–292).

Reflexes from carotid sinus important in the control of heart output

Reflexes originating in the carotid sinus have been shown by NHI scientists to control the vigor with which the heart's receiving chambers (atria) pump blood into the ventricles. This, in turn, importantly affects ventricular performance and cardiac output.

The carotid sinus has long been known to be sensitive to changes in blood pressure and to initiate nervous reflexes to compensate those changes. However, it was formerly thought that this was accomplished primarily by bringing about changes in peripheral resistance to blood flow and by reflexly changing heart rate. Now studies at the NHI Laboratory of Cardiovascular Physiology have revealed that when arterial pressure falls, the carotid sinus, in addition to reflexly increasing peripheral arteriolar and venous tone and heart rate, also increases the force of atrial contraction.

This is done by diminishing the activity of the vagus nerve (which normally restrains the atrial pulse) while simultaneously increasing the activity of the cardiac sympathetic nerves. Sympathetic stimulation increases the vigor of atrial contraction, presumably by increasing heart levels of catechol amines. These increase the excitability of the atrial muscle fibers and also the synchronization with which they contract.

The increased vigor of atrial contraction pumps more blood into the ventricle, distending it and elongating its muscle fibers more than usual. Since muscle fibers contract more forcefully from longer fiber lengths than from shorter ones (provided that the chemical environment of the fibers is not altered), the results is a more vigorous contraction of the ventricle and hence increased heart output.

The opposite takes place when arterial pressure is high. The carotid sinus reflexly increases vagus activity while decreasing sympathetic activity. This suppresses the atrial pulse, reducing ventricular filling pressure and decreasing heart output.

These reflexes, called the carotido-sympatho-atrial and carotido-vago-atrial reflexes, are held to be of substantial importance in the regulation of the circulation in changing states. They are particularly important at high heart rates, which give the ventricles less time to relax and the atria less time to fill them adequately between pumping strokes. By causing the atria to deliver more blood to the ventricles more rapidly under these conditions, these reflexes help to maintain the heart output at appropriate levels at high-heart rates.

The work leading to the discovery of the carotido-atrial reflexes was done by Drs. Stanley J. Sarnoff, J. P. Gilmore, and J. H. Mitchell. Their findings were reported at the Federation meetings in Chicago.

Alcohol causes deposition of fat in liver by action of pituitary

NHI scientists have found that large single doses of alcohol in rats, interfere with pituitary control over the fat transport system. As a result, excessive amounts of triglycerides (neutral fat) are mobilized from adipose tissue as free fatty acids and carried by the plasma to the liver, where they are recombined with glycerol and deposited in this organ. This derangement of fat transport may be important in the development of the cirrhosis often found in alcoholics, in which the chronic deposition of excessive fat in the liver is thought to lead eventually to necrosis.

Single orally administered doses of 4.8 grams of alcohol per kilogram of body weight (equivalent in humans to about six double martinis) resulted 18 hours later in a threefold increase in liver triglycerides in female rats. Larger doses increased liver triglycerides almost fivefold.

That these effects were due to the mobilization of fatty acids from adipose tissue rather than to an increased synthesis of fatty acids by the liver was shown by the linoleic acid content of the deposited fat. This unsaturated fatty acid cannot be synthesized by the rat, but is of dietary origin. When assayed by gas chromatography, the liver fat deposited by action of the alcohol was found to have virtually the same linoleic content as adispose tissue. Similar results were obtained when the oleic acid content was assayed. Since the concentration of both fatty acids in liver reflects that in adipose tissue, little if any of the fat deposited as a result of the alcohol could have come from fatty acids synethsized by the liver.

The finding that alcohol did not produce these effects in rats whose pituitaries had been removed suggested that the effects of alcohol on fat transport were mediated through hormones from this master gland. Investigation of the effects of alcohol on the pituitary-adrenal axis indicated that alcohol causes the pituitary to release ACTH and perhaps other hormones important in fat mobolization. However, the mechanism by which alcohol does so is not known.

The scientists found that pretreating rats with certain adrenergic blocking agents prevented the alcohol-induced fat deposition in liver, suggesting that the catechol amines may also be involved in the process. It is not yet clear whether the protection conferred by these agents is due to their blocking the action of amines at nerve endings which innervate fat cells or to their blocking the release of pituitary hormones. Studies of the mechanism or mechanisms involved are underway in the hope that these might lead to drugs that can prevent or ameliorate Laennec's cirrhosis.

The experiments were conducted by Drs. B. B. Brodie, H. M. Maling, W. M. Butler, Jr., and R. P. Maickel, of the Laboratory of Chemical Pharmacology, and by Dr. M. G. Horning, of the Laboratory of Cellular Physiology and Metabolism. Their findings were reported at the Symposium on Neurological and Hepatic Complications of Aloholism held in New York.

Myocardial edema result of high atrial pressure in congestive failure

Studies on the mechanism of myocardial edema—the accumulation of water and electrolytes in the heart muscle that often accompanies congestive heart failure—indicate that the major pathogenic factor is the elevated right atrial pressure also frequently found in this condition. Excessive serum levels of aldosterone, a hormone which promotes water and salt retention, and low serum protein levels may also play a role in the process.

The studies were performed on 46 dogs—21 normals and 25 with experimentally produced lesions causing chronic congestive heart failure or chronic ascites (accumulation of fluid in the abdominal cavity). After periods ranging from 6 to 189 days, the animals were anesthetized, sacrificed, and samples of heart tissue immediately taken for determination of water, fat, and electrolyte content.

The experimental data were then analyzed to evaluate the importance of the following factors in myocardial edema: the duration of heart failure, enlargement of the ventricles, serum aldosterone and protein levels, and elevation of right atrial pressure.

All of the experimental lesions produced moderate to marked increases in heart muscle content of water, sodium, and chloride. The observed increases in myocardial chloride suggested that the edema was the result of accumulation of extracellular fluid.

Comparison of data from dogs dying from heart failure within 6 days with data from another group surviving for 3 to 6 months ruled out duration of heart failure and ventricular enlargement as significant factors in myocardial edema. Other data suggested that high serum aldosterone and low serum protein levels, while not determining factors in themselves, do play supporting roles in the process.

The factor that appeared to be most important in myocardial edema was elevation of right atrial pressure. The degree of increase correlated well with the severity of the edema. Increased right atrial pressure appears to result in passive venous congestion, which, when combined with high serum aldosterone and low serum protein levels, leads to the accumulation of water, sodium, and chloride in heart muscle that constitutes myocardial edema.

These experiments were performed by Drs. N. A. Yankopoulos, J. O. Davis, Ernest Cotlove, and Mary Trapasso of the Laboratory of Kidney and Electrolyte Metabolism. Their findings were reported in the American Journal of Physiology (199: 603–608).

Neutral fat made in adipose tissue by mechanism similar to that in liver

NHI scientists have found that fatty acids are converted to their neutral storage form (triglycerides) in adipose tissue by a mechanism very similar to that reported by others for triglyceride synthesis in liver. The studies also indicate that the release of free fatty acids from adipose tissue may be importantly influenced by factors affecting the rate of triglyceride synthesis.

In these studies Drs. Daniel Steinberg, Martha Vaughan, and Simeon Margolis, of the Laboratory of Cellular Physiology and Metabolism, and Dr. Arthur Karmen, of the Laboratory of Technical Development, measured the conversion of a radioactive fatty acid (palmitic acid) to triglycerides and other neutral fat in rat adipose tissue. This tissue was ground up and the homogenized extract divided into two portions. One portion was then fortified with substances known to favor triglyceride formation; the other portion, unfortified, was used as the control tissue.

The incorporation of radioactive palmitic acid into neutral fat was observed only in the fortified tissue and was almost exclusively in the form of diglycerides and triglycerides. Knowing what substances had been added to the fortified tissue, the scientists were able to determine the probable sequence of biochemical steps by which triglycerides are formed in adipose tissue. This was found to be very similar to the sequence previously reported by others for triglyceride synthesis in liver.

Triglycerides, the form in which most fats are stored in the body, are neutral esters resulting from the combination of three fatty acid molecules with one molecule of glycerol. However, under the biochemical conditions of the body, this combination cannot occur directly. Instead, the fatty acids must first be combined with coenzyme A, which serves as a carrier in the process. Two of the combined molecules (fatty acyl-CoA) then react with glycerol, forming a diglyceride and regenerating coenzyme A. With coenzyme A again the carrier, the third fatty acid is added to the diglyceride to form the triglyceride. The triglyceride thus formed can in turn be broken down to yield its fatty acids to meet the body's energy requirements during the fasting state.

The scientists observed that the release of free fatty acids (FFA) from adipose tissue appeared to be influenced by the rate of triglyceride synthesis.

In the fortified tissue, where biochemical conditions favored triglyceride synthesis, there was a net uptake of FFA; however, in the unfortified tissue there was a net release of FFA. A number of hormones are known to stimulate FFA release, and these observations suggested that their action might be due in part at least to their effects on triglyceride synthesis.

In experiments following up this lead, Drs. Steinberg, Vaughan, and Margolis determined the effects of glucose, ACTH, epinephrine, and serotonin on triglyceride synthesis in intact adipose tissue incubated in a medium containing radioactive palmitic acid.

When glucose, an inhibitor of FFA release, was added to the incubation medium, the incorporation of the radioactive palmitic acid into triglycerides was more than doubled in the tissue sample. However, the addition of ACTH or epinephrine, hormones which stimulate FFA release, reduced triglyceride synthesis by 50 percent or more. The reduction in triglyceride synthesis was accompanied by increased FFA concentrations both in the tissue samples and in their incubation media. Serotonin, a hormone which does not affect FFA release, also did not affect the rate of triglyceride synthesis. These data thus lend support to the hypothesis that hormonal control over FFA release is exerted, at least in part, over the rate of triglyceride synthesis.

These findings were reported in Federation Proceedings (19: 227) and in the Journal of Biological Chemistry (235: 38–39).

Tranquilizer triggers pituitary-adrenal "stress" responses

Reserpine, a drug in wide clinical use as a hypotensive and tranquilizing agent, has been found to trigger certain body responses usually associated with stress: hypersecretion of ACTH, increased serum levels of glucocorticoids from the adrenal cortex, and excessive mobilization of free fatty acids from adipose tissue. The paradox implicit in these actions of reserpine is heightened by experimental evidence that these stress responses (1) are produced only by doses of reserpine sufficiently large to produce overt sedation, and (2) are the indirect result of the same action of the drug believed responsible for its tranquilizing effects—depletion of brain serotonin stores.

These findings were made by Drs. Bernard B. Brodie, Erik O. Westermann, and Roger P. Maickel, of the NHI Laboratory of Chemical Pharmacology, as part of a series of animal studies on the role of the hypothalmo-pituitary-adrenocortical system in biochemical adaptation. They were presented by Dr. Brodie at the Fourth International Neurochemical Symposium, held at Varenna, Italy.

The scientists found that doses of reserpine which which depleted brain stores of norepinephrine and serotonin, producing marked sedation, also provoked a sustained activitation of the pituitary-adrenal system. This activation was manifested in rats by (1) a fall in adrenal ascorbic acid, accompanied by a rise in plasma corticosterone; (2) increased activity of tryptophan peroxidase (TPO), a liver enzyme whose activity is an indicator of pituitary-adrenal stimulation; and (3) increased mobilization of free fatty acids from adipose tissue.

These responses are similar to those produced by the stress of prolonged exposure to cold, and were not produced by reserpine or cold in animals whose pituitaries or adrenals had been removed. This provided further evidence that these responses to reserpine result from pituitary-adrenal activation and are mediated by ACTH hypersecretion.

Hypersecretion of ACTH does not result from the action of reserpine per se, but is related to its depletion of brain serotonin stores. Doses of reserpine that deplete brain serotonin by less than 50 percent do not elicit noticeable sedation nor hypersecretion of ACTH; slightly larger doses elicit both responses, which become more marked with increasing doses until a maximum is reached with the complete depletion of brain serotonin stores. That ACTH hypersecretion is related specifically to serotonin depletion has been shown by experiments using alpha-methyl-m-tyrosine. Doses of this amino acid that depleted brain norepinephrine stores with very little effect on brain serotonin elicited neither sedation nor ACTH hypersecretion.

This indirect action of reserpine also explains why the stress responses, like the drug's sedative effects, persist long after the administered reserpine has disappeared. Apparently, reserpine is a hit-and-run drug which depletes the brain of amines by inactivating or destroying their storage sites. The brain amines remain depleted until the storage sites recover, when brain amines slowly return to normal. The stress responses will persist until brain serotonin again reaches 50 percent of normal.

These studies point out the potential value of pharmacological tools in clarifying how the brain directs biochemical mechanisms, and that the interaction of drugs with these mechanisms may be an important aspect of drug action.

Rheumatic fever studies reveal predictability of heart damage

NIH grant-aided studies of rheumatic fever recurrences at a rheumatic fever phophylaxis clinic indicate that (1) signs of heart valve damage in susceptible patients usually appear during the initial attack of rheumatic fever and (2) patients free from valvular involvement during the first attack usually remain free from rheumatic heart disease despite recurrent attacks.

These findings were reported in the New England Journal of Medicine (62: 533–540) by Drs. Alvan R. Feinstein and Mario Spagnuolo of Irvington House, Irvington-on-Hudson, N.Y., and the New York University College of Medicine in New York City.

There results are based on analyses of 370 documented attacks of rheumatic fever in 161 patients at Irvington House. Only those patients whose attacks fulfilled the modified Jones criteria for the diagnosis of rheumatic fever were included in the study.

The New York scientists found that valvulitis, as determined by careful stethoscopic examination, was a feature of the initial attack in 90 of these 161 patients.. With subsequent attacks, the valvulitis remained unchanged or became worse and in some cases was accompanied by cardiac enlargement, pericarditis, or congestive heart failure.

Valvular involvement was not found in the initial rheumatic episodes of 71 patients. With subsequent attacks, all but 10 of these patients remained free of valvulitis and other symptoms of heart disease. Although 10 patients were found to have a significant diastolic murmur at a subsequent attack, the investigators speculate that in at least 8 of these 10 patients, the murmur was present but not recognized at the first attack.

"The results suggest that the rheumatic host has a specific and persistent susceptibility to get or to avoid valvular involvement. If it does no occur with the first attack, it does not occur (with dubious exceptions) in the subsequent attacks. In most cases in which rheumatic heart disease develops, the valvular involvement is manifested in the very first attack," conclude Drs. Feinstein and Spagnuolo.

Their findings, which should be of considerable interest to the parents of rheumatic children, may enable a reduction in the duration of rheumatic fever prophylaxis for valvulitis-free patients. However, "Prophylaxis should not be stopped in this group without careful auscultatory confirmattion of cardiac status and until further studies confirm the present conclusions," state the scientists.

Lipids play major role in protein synthesis, NHI studies suggest

Evidence for a major role of intracellular lipids in protein synthesis has been gained from studies by Dr. Richard Hendler of the NHI Laboratory of Cellular Physiology and Metabolism. He reported these findings at the federation meetings.

In the search for the intermediate through which the stored genetic master plans for each protein molds and binds its amino acid structural units into the finished molecule, protein chemists in many countries are concentrating on variants of the nucleic acids, DNA and RNA. Genetic DAN, in the nucleus of the cell, is widely regarded as the storehouse for these master plans. RNA, located out in the microsomal structures of the cell, is widely regarded as a template, or die in which the protein is cast.

Dr. Hendler turned instead to the lipids, which he notes, are even more abundant than RNA in some of the miscrosomal structures thought to be sites of protein synthesis. (The ribosomes, riches of all in RNA, have been reported to contain about five times as much lipid as RNA.)

From studies of synthesis of the egg protein, albumin, by the hen oviduct, Dr. Hendler has gained evidence that the basic amino acid structural units of proteins combine with lipids very early in the protein assembly process to form more complex units (amino avid complexes). So far 11 albumin amino acids have repeatedly been seen to combine with the lipids in these complexes. The findings suggest the possibility that the lipid-associated amino acid groups may actually represent primitive precursors of the natural protein molecule.

From the evidence accumulated, Dr. Hendler speculates that the basic building blocks of the protein (the amino acids), arriving at the cell via the watery fluids of the body, are made fat soluble, entering into the lipid mechanism very early in the protein assembly process. It is in this lipid medium that their first orderly grouping seems to occur—perhaps the first step in the precise forging of the complex links (polypeptides) that will make up the great chains of the finished protein.

Dr. Hendler is also considering the possibility that the whole assembly process—genetic master plan to emergence of the finished molecule—is a lipid process, the study of which might fill major gaps that remain in current understanding of how proteins are made. With this as a working hypothesis, he is continuing in his attempts to sift out recognizable protein precursors in new lipid-associated amino acid complexes.

He is also hoping to find the chemical process by which the individual amino acids are made fat soluble, for this might be the key step which introduces the raw materials of the protein—the amino acids—into the cell's machinery for making the protein.

Myosin molecule consists of three tightly coiled protein chains

Recent advances in protein chemistry at NHI and elsewhere permit the conclusion that the myosin molecule is made up of three identical chains, each wound in a tight coil and all three twisted together as a long rope.

The protein myosin is of interest in terms of cardiovascular functions because it is believed to be the predominant component of the contractile system of muscle. A program of research on myosin at NHI has the immediate objective of interpreting some of the properties of myosin on the basis of its molecular structure, and is ultimately aimed at understanding its role in the contraction of muscle.

Like other proteins the myosin molecule is made of amino acid groups, bound together as links in the long chains which constitute its primary structure. Although myosin is known to be a comparatively long slender molecule (1,600 x 22 Angstrom units), it has not been known how many polypeptide chains are held together by secondary bonds to form the molecule and, if more than one chain, whether or not they differ from one another.

Drs. W. Wayne Kielley and William F. Harrington, in the NHI Laboratory of Cellular Physiology, have approached this problem using guanidine hydrochloride to break the secondary bonds holding the chains together, while leaving intact the primary bonds holding together the polypeptide links of each chain.

Examining the products of this dissociating process by sedimentation in the ultracentrifuge, together with observations of their diffusion rates, viscosities, optical rotation properties, and other data, the investigators have concluded that the myosin molecule consists of three identical polypeptide chains, each wound into a tight helical coil, the three chains themselves being wound together in the form of a long rope.

These findings were published in Biochimica et Biophysica Acta (41: 401–421).

Nature of hormone control over fatty acid release explored by NHI studies

Recent studies at the National Heart Institute have explored the mechanisms whereby fatty acids are stored in the body's fat depots as triglycerides (neutral fat) or are released from these depots as unesterified fatty acids (UFA) to meet the body's energy requirements. The studies sought to clarify the mechanism or mechanisms by which four hormones—epinephrine, norepinephrine, ACTH, and glucagon—stimulate UFA release from adipose tissue.

Triglycerides, the form in which most fats are stored in the body, are neutral esters formed by the combination of three molecules of fatty acid with one molecule of glycerol. The triglyceride can in turn be broken down to yield three molecules of UFA, an important metabolic fuel during the fasting state. The latter process is known to be subject to a number of hormonal controls.

Seeking to clarify the nature of these hormonal controls, Dr. Martha Vaughan, of the Laboratory of Cellular Physiology and Metabolism, studied the effects on adipose tissue of four hormones shown by others to stimulate the release of UFA: epinephrine, norepinephrine, ACTH, and glucagon. Using rat adipose tissue incubated in a medium containing albumin and glucose, Dr. Vaughan found that hormonal stimulation of UFA release was accompanied by increased uptake of glucose by the tissue and by stepped up phosphorylase activity.

Phosphorylase is an enzyme which breaks down glycogen, the form in which carbohydrates are stored in the body, to yield glucose, an important energy source. In the liver, the resulting glucose can be released into the blood by action of the enzyme phosphatase. However, the phosphatase is not present in adipose tissue, so that the small amounts of glucose resulting from phosphorylase activity must be used locally, either as a source of energy or for conversion into fatty acids and triglycerides.

The fact that all four hormones stepped up phosphorylase activity at the same time that they stimulated UFA release suggested that the hormones might control UFA release by a common mechanism. Phosphorylase is not the common denominator, however, since previous work at this laboratory had shown that serotonin, a hormone which increased phosphorylase activity, did not stimulate UFA release.

But the increased phosphorylase activity produced by ACTH in adrenal tissue and by epinephrine and glucagon in liver does have a common denominator—cyclic 3,5 adenylic monophosphoric acid. The hormones have been shown by others to stimulate the accumulation of this compound, which in turn increases active phosphorylase. It is probable that the compound may play a similar role in adipose tissue in the intact animal, even though the compound produced no demonstrable effects on phosphorylase in the in vitro studies.

It is also possible that 3,5 AMP may play a role in hormone-stimulated UFA release, perhaps by affecting reactions in addition to that producing increased phosphorylase.

These findings were reported at the meeting of the American Society of Biological Chemists.

Active ion transport in red cell ghost powered by ATP

Studies by Dr. Joseph Hoffman, of the NHI Laboratory of Kidney and Electrolyte Metabolism, have shown that Adenosine triphosphate, a compound that powers many of the body's energy-consuming processes, is also the direct energy source for active ion transport in the red blood cell. His findings were reported at the federation meetings.

Active ion transport is the process whereby the cell can actively and selectively transport electrically charged substances (ions) across the cell membrane against opposing electrochemical forces. In this process, the "ion pump" maintains normal electrolyte balance within the cell by using ATP generated by cell metabolism to offset the loss of ions across the cell membrane by passive diffusion.

Presumably because one ion cannot replace the metabolic functions of another, the cell must maintain the proper concentrations of the proper ions both for the regulation of its volume and for its metabolic operations. This would be impossible but for the delicate balance struck between passive loss on the one hand and active transport on the other.

Previous work on intact red blood cells by Dr. E. T. Dunham, formerly of the same laboratory, had indicated that ATP might be the fuel for the ion pump. In studies following this lead, Dr. Hoffman used red cell "ghosts" whose normal contents had been considerably reduced by hemolysis. The ghosts not only retained the membrane characteristics of the intact cell, but could also be reconstituted containing known substances whose metabolism could subsequently be observed without the interference that might result from other metabolites and metabolic processes in the intact cell.

Dr. Hoffman's studies showed that ATP was the specific fuel for the ion pump in the ghost system; however, if no ATP was incorporated into the ghost, the pump would still work (though less efficiently) if other substances that would generate ATP were incorporated. These findings suggest that the ion pump requires the presence of an enzyme (an ATPase) in order to use ATP. Such an enzyme has been characterized in membranes isolated from red blood cells by Dr. R. L. Post of Vanderbilt, and appears to possess the same activation characteristics as does active ion transport in both red cells and other ghosts. Thus the evidence is strong that the ion pump either is an ATPase, or else has an ATPase as an intimate component.

Protein and fat fractions of lipoprotein molecule provided by liver

Scientists at NHI have found that the liver, previously shown to be the source of the lipid portion of lipoproteins, is also the source of the protein of this complex molecule, the form in which fats are transported in the blood. Experiments conducted by Drs. Charles Radding and Daniel Steinberg, of the Laboratory of Cellular Physiology and Metabolism, have demonstrated that rat liver slices, incubated in vitro, synthesize and secrete high-density lipoproteins identical with those found in normal rat serum. Their findings are reported in the Journal of Clinical Investigation.

The liver slices were incubated in rat serum with a complete mixture of amino acids labeled with carbon-14. After incubation periods ranging up to 4 hours, the slices were removed and samples of the media ultracentrifuged to separate the lipoprotein fractions. These were then analyzed by the "fingerprint" technique.

When broken down by the proteolytic enzymes trypsin or chymotrypsin, each protein yields its own characteristic peptide degradation products. These can be spotted on filter paper and separated on the vertical axis by descending paper chromatography, then on the horizontal axis by electrophoresis to form a characteristic peptide pattern. When this pattern is developed by ninhydrin staining, the result is a distinctive "fingerprint" which identifies the protein.

The ninhydrin fingerprints of high-density lipoproteins from the incubation medium were compared with fingerprints of lipoproteins of the same density class from normal rat serum and found to be identical. Autoradiograms (made by placing the media fingerprint strips in contact with X-ray film for 1–2 months, then developing the film) showed the presence of radioactivity in all of the ninhydrin spots of the fingerprint.

These comparisons showed that the lipoproteins synthesized by the liver slices were identical to those of normal serum; and, since labeled amino acids had been incorporated into all of the newly synthesized lipoproteins, that the liver was the source of the protein as well as the lipid portions of those lipoproteins.

To determine whether the rate of lipoprotein synthesis is affected by the rate of cholesterol synthesis, the scientists pretreated rats to speed up or slow down their cholesterol production. Liver slices from these rats were then incubated with acetate (a cholesterol precursor) and an amino acid, both tagged with radioactivity so that the rates of cholesterol and lipoprotein synthesis could be measured simultaneously.

Lipoprotein synthesis was not noticeably affected even by wide variations in the rate of cholesterol synthesis in these experiments, which suggested that the two rates were independent of one another. This was not proved conclusively, however, because of the possibility that enough cholesterol might already have been formed in the tissue before incubation was begun to support normal rates of lipoprotein synthesis during the short period of experimental observation, but not over extended periods.

Other experiments showed that liver slices from nephrotic rats synthesized both lipoproteins and other serum proteins more rapidly than did those from normal rats. This suggests that overproduction of lipoproteins may be an important factor in the hyperlipemia of nephrosis.

Observe accelerated drug metabolism in pretreated rats

Pretreating rats with a variety of drugs has been found by NHI scientists to increase the activity of drug-metabolizing enzyme systems in the liver, thus decreasing the duration of drug action in the body.

The findings were reported in the "Federation Proceedings" (19: 390) by Drs. A. H. Conney, I. A. Michaelson, and J. J. Burns of the NHI's Laboratory of Chemical Pharmacology. This Laboratory is conducting a broad program of basic studies aimed at elucidating the factors regulating duration of drug action. Previous studies in this Laboratory had shown that special enzyme systems in liver microsomes, tiny particles in liver cells, inactivate many drugs as well as other compounds foreign to the body by converting them into compounds which the kidney can excrete.

In the currently reported studies, Dr. Conney and coworkers investigated the ability of microsomal enzyme systems in rat livers to metabolize several commonly used drugs following repeated doses of the same or another drug. Rats were pretreated for 4 days and their livers incubated with test drugs to determine microsomal enzyme activity. The scientists also tested enzyme activity in live, pretreated rats by measuring the duration of action of test drugs. Drugs used in the study included barbiturates, muscle relaxing drugs, analgesics, antirheumatic agents, a carcinogenic hydrocarbon, and an antihistamine.

Results of the liver incubation studies showed that pretreatment with phenobarbital, barbital, phenylbutazone, orphanedrine, or aminopyrine caused severalfold increases in the ability of liver microsomes to metabolize hexobarbital, zoxazolamine, phenylbutazone, and aminopyrine, report the investigators. They obtained evidence of accelerated drug metabolism in living, pretreated rats by demonstrating a shortened duration of action of hexobarbital, zoxazolamine, meprobamate, and carisoprodol in animals that had received repeated doses of these drugs.

In other in vitro studies, the investigators observed that pretreatment with the hydrocarbon, 3,4-benzpyrene, stimulated the microsomal enzyme system that metabolizes zoxazolamine, but not the hexobarbital-metabolizing system. "In accord with this, 3,4-benzpyrene administration shortens the duration of zoxazolamine paralysis from 730 minutes to 17 minutes but does not shorten the duration of hexobarbital hypnosis," they report. Interestingly, the duration of action of both zoxazolamine and hexobarbital was shortened in rats pretreated with the antihistaminic drug, chlorcyclizine.

"The findings that pretreatment of animals with one drug can speed up the metabolism of the same or another drug may be of considerable importance when evaluating the pharmacological activity of drugs that are given repeatedly, either alone or in combination," stated the Heart Institute scientists.

Prednisone-aspirin equally effective in preventing rheumatic heart damage

Cooperative clinical studies have shown that large doses of the steroid, prednisone, are not superior to therapeutic doses of acetylsalicylic acid (aspirin) in preventing residual rheumatic heart disease. The NHI grant-aided studies were conducted by the Combined Rheumatic Fever Study Group which consists of 12 investigators in children's cardiac services of 8 hospitals: 4 in New York City, 2 in Baltimore, and 1 each in Boston and Cleveland. The investigators, coordinated by Dr. A. G. Kuttner, of New York University-Bellevue Medical Center, report their combined findings in the New England Journal of Medicine (262: 895–902, 1960).

Their findings are similar to those of an earlier cooperative study of aspirin versus steroid therapy, sponsored jointly by the Research Council of Great Britain and the American Heart Association. In the present study, however, steroids were given in larger doses and over a longer period of time.

Admitted to the study were 57 patients who met the following criteria: (1) They were 12 years of age or younger, (2) had suffered their first attack of rheumatic fever not more than 28 days previously, and (3) had moderate to severe carditis as evidenced by pericardial rub or effusion, cardiac enlargement, congestive heart failure, and/or significant heart murmurs. About half of these patients received large daily doses of prednisone which totaled 3 grams over a 12-week treatment period; the remaining patients were given doses of acetylsalicylic acid sufficient to maintain blood levels at 25 to 35 mg./100 cc., also for a 12-week period. Three weeks after termination of therapy and again 1 year later all patients were reexamined and the incidence of residual heart disease in each group compared.

The study group found that both prednisone and aspirin controlled acute rheumatic symptoms in most patients, and, during the ensuing year, all patients remained free of rheumatic recurrences. Of those patients available for study at the end of the year, 12 in the prednisone group and 16 in the aspirin group recovered completely with no signs of residual rheumatic heart disease, whereas 16 prednisone and 7 aspirin-treated patients had residual heart disease at this time. Of three patients originally allocated to the aspirin group but later switched to prednisone, one recovered completely and two were left with residual heart disease.

Thus, "large doses of prednisone given for 12 weeks were not found to be superior to acetylsalicylic acid in preventing residual rheumatic heart disease," conclude the investigators. "The chief action of both prednisone and salicylates appears to be to suppress the inflammatory reaction caused by this disease. In many patients, however, even if the acute symptoms are promptly and well controlled, cardiac damage is not prevented," they state.

In view of these findings, all but one of the investigators felt the risk of prolonged steroid therapy was unwarranted, although no serious side effects of prednisone were noted in this study.

PROGRAM HIGHLIGHTS

Weeklong graduate course in cardiovascular disease given at Heart Institute

"Current Research in Cardiovascular Disease," a 1-week postgraduate course sponsored by the American College of Physicians, was given at the National Heart Institute in May. One hundred and fifty physicians attending the course came from a widespread area, with almost every State in the Union being represented, as well as Canada and Puerto Rico. Nine physicians from the PHS Division of Hospitals attended as guests of the Heart Institute and as part of its cardiovascular training program.

Dr. Luther L. Terry, Assistant Director, NHI, directed the course, and 42 Heart Institute staff members participated.

Focused around the research program of the Heart Institute, the course was aimed at acquainting internists with some of the many facets of cardiovascular disease currently under investigation. The faculty discussed the research most applicable to clinical medicine, and supplemented this material with background information and reports on related work in other institutions.

Flu vaccine recommended for heart patients by NHI and AHA

In October the National Heart Institute and the American Heart Association publicized the need for routine vaccination against influenza for persons with heart and blood vessel disease. The action was taken in support of a PHS program to intensify efforts to encourage vaccination of selected population groups where hazards from influenzal infections are particularly great.

A joint statement released by Drs. A. Carlton Ernstene, president, AHA, and James Watt, Director, NHI, reads:

"The epidemics of influenza which occurred in the fall of 1957, the spring of 1958, and the first quarter of 1960 have again emphasized the fact that individuals with cardiovascular or pulmonary disease are more susceptible to the hazards of influenza than is the general population. The increased risk is shown both by more severe illness and by higher fatality rates among patients with these diseases

"Evaluation studies with influenza virus vaccine have shown that its use is of definite value in preventing influenza.

"In adults, side reactions have been extremely few and use of the vaccine is contraindicated only in those patients who are allergic to components of the vaccine. The Public Health Service Advisory Committee on Influenza Research has strongly recommended that those persons at high risk of death from influenza obtain immunization as a protective measure. Because influenza epidemics recur in unpredictable cycles, and particularly because some influenza occurs continually, annual immunization has been recommended.

"The American Heart Association and the National Heart Institute wish, therefore, to bring these facts to the attention of all physicians. In addition, it is urged that persons with cardiovascular disease consult their physician as to the advisability of obtaining routine influenzal vaccination."

Primate station underway at University of Oregon; strong interest noted

Construction began during 1960 of the first regional subhuman primate research center under the new primate and veterinary grants program. Located near Portland, Oreg., the center is being built with funds from an NIH grant of $1,792,000. A separate grant of $125,275 was awarded at the same time for initial operation of the center. Principal investigators are Donald E. Pickering, M.D. and Edward S. West, Ph. D., both of the University of Oregon Medical School faculty.

Other primate research centers are planned, at locations to be selected in the near future. Since the beginning of the program in 1959, following a special congressional allotment of Heart Institute funds for construction and initial operation of the centers, a number of grant applications have been received from interested scientific groups at various universities.

The new centers are intended to provide ideal enviroments where both resident and visiting scientists, representing a breadth of disciplines, may pursue research that will advance all areas of knowledge relating to the biological characteristics of the primate throughout its entire life span. The centers will offer opportunities for fundamental research as well as studies more directly related to a variety of human diseases.

Scientific exchange program begun with Soviets by Heart Institute

Four Soviet physicians visited NHI in May to participate in planning a joint program of scientific cooperation in the field of heart disease. Their 2-week visit included talks with officials and consultants of the Heart Institute, and a tour of scientific institutions in Bethesda, Baltimore, Boston, Cleveland, and New York.

Following Chairman Khrushchev's 1959 visit, the United States and the U.S.S.R. signed an agreement (November 21, 1959) for cooperation in the scientific, technical, and cultural fields. Under the public health and medical sciences portion of the agreement, the U.S.S.R. Ministry of Health and the U.S. Public Health Service were directed to facilitate cooperation between research organizations in the two countries on various important problems of medicine. In the area of cardiovascular disease, the two institutions designated were NHI and the Institute of Therapy, Academy of Medical Sciences, Moscow.

The meetings were considered highly fruitful by members of the two groups, and a number of agreements were reached.

The NHI and the Institute of Therapy each agreed to prepare a list of subjects and areas in which they are particularly interested in exchanging workers. A specific person was to be selected by each side to serve as the focus for exchanges in a particular disease area.

Recognizing the importance of nomenclature and classification of cardiovascular diseases, each side agreed to prepare material and suggestions on this subject.

Each side also agreed to proceed with plans for the exchange of individual workers, and to speed and increase the exchange of medical journals, books, and films.

The Russian party, headed by Dr. Alexander Myasnikov, director of the Institute of Therapy, Academy of Medical Sciences, Moscow, included: Dr. Ivan Speranskiy, vice director of the Institute of Therapy, Academy of Medical Sciences, Moscow; Dr. Mariya Bavina, biochemical laboratory in the Institute of Therapy, Academy of Medical Sciences, Moscow; and Dr. Nodar Kipshidze, member of the Academy of Medical Sciences, and professor and head of the faculty of Therapy Clinic, Tbilisi. Dr. Boris Ilinskiy, therapy section, Institute of Physiology, Pavlov Academy of Science, Leningrad, was unable to come due to illness.

The U.S. participants, headed by Dr. James Watt, Director, National Heart Institute, included Dr. Paul D. White, emeritus clinical professor of medicine, Harvard Medical School, Boston; Dr. E. Cowles Andrus, associate professor of medicine, and chief, division of cardiology, department of medicine, Johns Hopkins Hospital, Baltimore; Dr. George E. Burch, chairman, department of medicine, Tulane University School of Medicine, New Orleans, La.; Dr. Michael E. De Bakey, chairman, department of surgery, Baylor University, Houston; Dr. Irvine H. Page, director of research, Cleveland Clinic, Cleveland; Dr. David D. Rutstein, professor and head, department of preventive medicine, Harvard University Medical School, Boston; Dr. Luther L. Terry, Assistant Director, National Heart Institute, Bethesda; Dr. Robert W. Wilkins, professor of medicine, Boston University School of Medicine, Boston; and Dr. Irving S. Wright, professor of clinical medicine, Cornell University Medical School, New York City.

Later in the year, Dr. Luther L. Terry, Dr. Paul D. White, and Dr. E. Cowles Andrus met again with members of the Russian heart delegation, following the Third European Congress of Cardiology in Rome. Discussions were held of the material that had been exchanged dealing with classification and nomenclature of atherosclerosis, ischemic heart disease, and hypertension. Also discussed were future information exchanges and possible cooperative studies.

NHI continued support and participation in scientific meetings

NHI contributed substantially in 1960 to world medical and scientific communication through participation in, and grant support of, conferences, symposia, and workshop sessions preparatory to conferences. The meetings afforded invaluable opportunities for the interchange of scientific information, as well as for the planning of collaborative studies and new projects.

Seven of the scientific meetings were held outside the United States with the Heart Institute providing travel and maintenance funds for some participants, and contributing toward operating expenses, such as rent for conference rooms, simultaneous translation and public address systems, printing expenses, and recordings of proceedings. NHI aided in making five of the U.S. meetings international in character by providing funds for travel and maintenance of foreign as well as American participants.

Major NHI-aided conferences of the year were: (1) A conference on thrombolytic agents, Chicago, April 8–9; (2) a symposium on the pathogenesis of essential hypertension, Prague, Czechoslovakia, May 22–29; (3) the Second Asian-Pacific Congress of Cardiology, Melbourne, Australia, May 31–June 3; (4) the Fifth International Congress of Gerontology, San Francisco, August 7–12; (5) the Sixth Interamerican Congress of Cardiology, Rio de Janeiro, August 14–20; (6) the First International Congress of Nephrology, Evian, France and Geneva, Switzerland, September 1–3; (7) two international congresses in Tokyo on hematology, September 4–10, and blood transfusion, September 12–15; (8) a conference on prosthetic valves for heart surgery, September 9–10; and (9) a conference on thrombolytic activity and related phenomena, Princeton, September 18–21.

Three of the foregoing had NIH study section sponsorship. The hematology study section sponsored the Chicago Conference on Thrombolytic Agents, and was a joint sponsor with the international committee on blood clotting factors of the Princeton Conference on Thrombolytic Activity and Related Phenomena. The Conference on Prosthetic Valves for Heart Surgery was sponsored by the surgery study section.

WEDNESDAY, MARCH 29, 1961.

NATIONAL INSTITUTE OF DENTAL RESEARCH

WITNESSES

DR. FRANCIS A. ARNOLD, DIRECTOR, NATIONAL INSTITUTE OF DENTAL RESEARCH

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. LUTHER L. TERRY, SURGEON GENERAL

HARRY L. DORAN, CHIEF FIANCE OFFICER

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	936	1, 234	1, 546
Positions other than permanent	17	18	57
Other personnel compensation	10	8	6
Total personnel compensation	963	1, 260	1, 609
12 Personnel benefits	44	68	86
21 Travel and transportation of persons	53	80	88
22 Transportation of things	4	10	12
23 Rent, communications, and utilities	21	32	35
24 Printing and reproduction	4	2	4
25 Other services	36	58	69
Payment to "National Institutes of Health management fund"	543	721	826
26 Supplies and materials	100	154	237
31 Equipment	78	862	85
41 Grants, subsidies, and contributions	6, 157	9, 450	9, 989
Subtotal	8, 003	12, 697	13, 040
Deduct quarters and subsistence charges	5	5	5
Total obligations	7, 998	12, 692	13, 035

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	151	211	237
Full-time equivalent of other positions	3	2	8
Average number of all employees	142	168	217
Number of employees at end of year	163	202	233
Average GS grade	6. 4	7. 0	7. 0
Average GS salary	$5, 348	$6, 064	$6, 069

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(a) Research	4,418	5,725	5,938
(b) Fellowships	650	760	760
(c) Training	1,100	2,965	3,291
Total, grants	6,168	9,450	9,989
2. Direct operations:			
(a) Research	1,524	2,695	2,628
(b) Review and approval of grants	197	260	277
(c) Administration	95	127	141
Total, direct operations	1,816	3,082	3,046
Total program costs	7,984	12,532	13,035
3. Relation of costs to obligations: Obligations incurred for costs of other years, net	14	160	
Total obligations	7,998	12,692	13,035
Financing:			
Comparative transfers to other accounts	1,970	2,150	
Unobligated balance lapsing	51	658	
New obligational authority (appropriation)	10,019	15,500	13,035

GENERAL STATEMENT

Mr. FOGARTY. The committee will come to order.

We have before us at this time the request of the National Institute of Dental Research. Dr. Arnold, it is good to see you back.

At this point in the record we will insert the detailed statement which covers this request.

(The statement follows:)

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF DENTAL RESEARCH, PUBLIC HEALTH SERVICE

Mr. Chairman and members of the committee, the following statement will review for this committee progress made by the National Institute of Dental Research as it endeavors to advance general health through the study of oral diseases.

Of all avenues leading to the prevention of disease the one offering the greatest hope is research. Thus in the span of a little more than a decade, the investigative program of the Institute has grown and matured through its research approach to the oral diseases within the framework of all the biological and medical sciences. In the coming year this momentum will be further accelerated by occupancy of the new dental building—a long awaited privilege that will confer still greater dimension to the intramural research program of the Institute.

Considerable attention has been given in the past year to the formulation of plans for the best utilization of scientific manpower and equipment. This undertaking has necessarily involved a careful reappraisal of current progress, so as to better envision the design of promising new programs. For example, an intimate knowledge of enzymes has obvious implication for all biological processes, particularly those manifested in the oral cavity. To gain further insight into the essential structures and catalytic mechanism of enzymes, a section on enzyme chemistry was established during the year. The present nucleus of this activity is programed for limited expansion immediately following our move to the new building this spring.

Another newly instituted program activity is concerned with the anatomy and physiology of the mouth and pharyngeal region, and with distortions of form and function resulting from congenital anomalies or neurological disorders. Inasmuch as the major purpose of this program is to provide a continuous interaction of studies of the normal developing human, the impaired human, and normal and experimentally impaired animals, the personnel involved will engage in various interests. These will include the application of available methods of pressure and sound recording (electromyography, cinematography, and cinefluorography) to functions of respiration, feeding, and speech in subjects with orthodontic deformities, neurological impairments of the mouth and pharynx, and defects such as cleft palate. The very nature of these impairments dramatically emphasizes the role of the mouth and its adjacent structures in the formulation of speech and in the maintenance of essential life processes of respiration and nutrition. Viewed in such logical perspective, the oral cavity is as much a vital organ as the heart, liver, or lungs.

The already proven value of the germfree animal in identifying micro-organisms pathogenic to oral tissues dictates high priority for the early expansion of this activity. Other areas of proposed expansion include those of experimental embryology and immunology. This latter unit will, for example, conduct research in host defense against infectious diseases of the mouth; and, study allergic reactions to a variety of local anesthetic agents, antibiotics, and prosthetic materials used in everyday dental practice.

Although the expanded horizon of dental research at the Institute and indeed in many dental schools, implies an increasing availability of well-trained young scientists, the unfortunate facts are that dentistry, like most health professions, must compete for scarce manpower. Backgrounding this are the pressures for service arising from a burgeoning population. From the recently completed survey of Dentistry in the United States by the American Council on Education, we learn that Americans now have about 700 million untreated cavities—an average of nearly 4 each. By age 50 about half of the U.S. population has developed the periodontal disorders which among adults cause more tooth loss than is caused by decay. Moreover, by age 65 the incidence of this disease approaches 100 percent. Thousands of persons have other correctable oral problems that go undetected and untreated. In meeting these needs the average practicing dentist can care for about 1,000 patients per year, yet the dentists population ratio today is nearly twice that or 1 to 1,900 persons. These figures are a stark reminder that our profession must be frugal in budgeting its total available manpower to insure an adequate number of clinicians now and in the future.

Viewing the other side of the coin we know, for example, that one dental scientist, if he should discover a means of preventing or reducing tooth decay might do more for oral health than several thousand practitioners of restorative dentistry. A case in point, of course, is the discovery of fluoridation with its proven ability to reduce tooth decay by more than 65 percent. Thus, there is certainly great urgency to divert more total manpower into those fields of research where a collection of inquisitive minds may multiply the chances for new knowledge leading to scientific breakthroughs.

The best laid plans and aspirations for more practitioners and research workers are based, in the final analysis, on the capacity and ability of our dental schools to train adequate numbers of graduates skilled in both the art and science of dentistry. It is to this general area of interest that I would like to address special comment, particularly with respect to research and teaching manpower needs that are mounting at a rate of about 500 trained individuals a year. Dental schools listed on their faculty rolls last year some 5,500 teachers. Of these, about 4,300 were attached directly to dental schools—the others were mostly basic science teachers affiliated with medical schools. Of those teachers who were members of dental faculties, 74 percent were practicing dentists teaching only on on a part-time basis. Thus, in effect, the 4,300 listed teachers were equivalent to only 1,878 full-time teachers. While the intellectual stimulus that the successful practitioner can bring to the academic scene is desirable, it is not without significance that over half of these individuals consider practice, not teaching, as their careers.

Foremost in our armamentarium of support for the deficient areas of dentistry are fellowships and training grants to establish and nourish graduate training centers at dental schools, hospitals, and other institutions having an interest in dentistry. Thus far in 1961, the Institute has already awarded a little over $1 million to 26 institutions to finance 115 trainees. Also, a number of grants were made to dental schools with smaller research potential to permit them to send young faculty members to research centers with the expectation that they will return to their home institutions to become the nucleus of a research program.

The past year has witnessed much in the way of research progress both in the intramural and extramural programs of the Dental Institute. I would like at this time to share with you some of the highlights of this progress.

INTRAMURAL RESEARCH

The dean of a leading eastern dental school was quoted in the survey of "Dentistry in the United States" as saying: "If all the dentists in the United States were lined up on the east coast and moved westward, taking care of the needs of our population, by the time they reached Harrisburg, Pa., they would have to go back and begin all over again."

Thus, of necessity, the field of preventive dentistry is brought into even sharper focus with each passing year, and emerges in 1962 as the prime target for research in the Bethesda laboratories of the Institute. The goals around which our programs are polarized today have evolved in the short span of three decades from the small Dental Hygiene Unit established by the Public Health Service in 1931. Staffed by only one dental officer, its primary function was to apply principles of epidemiology to a series of community studies on mottled enamel. This activity was later expanded into a full-scale epidemiological program designed to document the effectiveness of fluoridation as a caries control measure.

Beginning in 1936, the dental research program was further broadened to include animal studies on the physiology and toxicology of fluoride compounds. As might be expected, many of these investigations led away from fluoride and into basic research on the causes and prevention of a variety of diseases involving the teeth and supporting structures. Today, on the eve of transition from very limited facilities to the modern, well-equipped new building at the National Institutes of Health, we (and here I speak for each member of our professional staff) are indeed grateful for the opportunity to provide an even greater manifold approach to better oral health.

Bacteria and dental decay

In our Laboratory of Microbiology we are continuing to use the germfree method of study for testing the pathogenic effects of oral bacteria alone and in combinations. Previous studies at the University of Notre Dame had provided dental scientists for the first time with positive evidence that dental decay does not occur in the absence of bacteria. Recently our investigators have shown that dental caries can be induced in the germfree rat by infecting them with a single strain of streptococcus bacteria isolated from dental caries from conventional rats. Following these observations our workers found that caries developed in the normally caries-free albino hamster when another type of streptococcus, isolated from decay lesions in the golden hamster, was implanted in the oral cavity. Somewhat unexpected was the significant observation that cariogenic streptococci from the rat had no adverse effect on the teeth of the hamster, and some of the seemingly identical strains were noncariogenic in the rat. Furthermore, none of several strains of lactobacilli—an organism commonly associated with caries in humans—has proved to be cariogenic in germfree experiments. Should these preliminary observations be confirmed by more extensive investigation, presently held concepts that dental caries in humans can be caused by a variety of micro-organisms would need reappraisal. If human caries is also found to be caused by a single, or only a few specific micro-organisms, the problem of its eventual control will be greatly simplified. One obvious possibility, although purely conjectural, would be the development of an anticaries vaccine or a specific chemotherapeutic agent.

Bacteria and tartar formation

Another significant development from the Institute's germfree laboratories was the discovery that dental calculus, long associated with oral bacteria, can occur in the total absence of bacteria. Previous studies at the Institute had suggested the occurrence of tartar-like deposits in germfree mice. This observation was recently confirmed in studies which proved, with X-ray diffraction analysis, that the crystalline component of tartar formed on the molar teeth of germfree rats was identical to that seen in conventional animals and in humans. As a result of this research lead, our scientists are now directing increased attention to biochemistry as a possible means of explaining the formation of tartar—a contributing factor in the development of periodontal disease.

Chemical agents for the control of dental decay

With information now available on the mode of caries infection, and the identification of involved bacterial pathogens, Institute investigators were able in the past year to begin a systematic search for chemical inhibiting agents that interrupt or alter the metabolism of selected strains of the oral bacteria. While most antibiotics are effective depressing agents, they usually suppress the entire oral flora. In addition, undesirable features such as antibiotic sensitivity and the development of antibiotic resistant organisms limit their practical use as cariostatic agents. However, chemical agents tested to date include three organic compounds that have produced a significant reduction in animal caries by interrupting the normal growth process of various oral bacteria. Screening programs such as these are considered by dental investigators to be an important prerequisite to clinical trials in humans.

Scientists in our Laboratory of Biochemistry have shown that dental decay in animals is markedly reduced by adding certain mineral phosphates to the diet. An extension of these experimental findings to humans is now being sought in large-scale clinical studies to assess the effects of dicalcium phosphates on caries in children. Concurrent with the clinical trials now underway in the Midwest are laboratory studies to determine how these compounds alter the decay process. There is reported evidence that the solubility of the mineral compound is an important factor. For example, highly insoluble phosphates are noncariostatic, whereas the very soluble forms, particularly sodium and ammonium phosphate, are extremely effective. Although the exact mode of action is still obscure, our people believe that some fundamental inhibitory reaction may be occurring locally, perhaps on the exposed surfaces of the teeth.

Along with consideration of the several mineral phosphates, the cariostatic effect of an organic phosphate, sodium phytate, was also investigated this year by Institute workers. They found, for example, that when rats were fed an otherwise cariogenic diet containing sodium phytate, the reduction in dental decay was considerably greater than that achieved with either sodium or ammonium phosphate. This dramatic caries inhibition was unexpected because phytate is hydrolyzed primarily in the lower intestine. Moreover, data from serum analysis of blood from animals receiving sodium phytate confirmed the presence of available phosphorus, thereby suggesting a cariostatic effect of possible systemic origin.

Chemical regulators in calcification

Many interesting reports have appeared recently on the subject of calcification. A high percentage of these reports reflect the work of scientists who would like to know more about the underlying process of mineralization of our body tissues. For example, why do bones and teeth calcify and become hard, while other tissues such as skin or tendon do not? Basic studies bearing on this subject have suggested that chemical "regulators" operating at the cellular level may be an important factor that influences or even controls the mineralization of certain body tissues. A unique method for exploring further the existence of such regulators and the relationship of collagen to mineralization in living animals was reported this year by our scientists who implanted strips of rat tail tendon as a source of collagen in the peritoneal cavity of young laboratory animals. They found that these so-called noncalcifying collagenous tissues removed after several months, had undergone mineralization and were hard on gross examination. True calcification was later confirmed by electron diffraction analysis. This phenomenon of "intraperitoneal mineralization" has given rise to challenging possibilities for animal experimentation. For example, purified collagen preparations may now be subjected to various treatments prior to implantation; or, be implanted in combination with agents thought to influence mineralization. Research workers believe that such living "model systems" operating under controlled conditions will provide valuable information on the little understood process of calcification.

Emotional stress and oral disease

Recognizing the need for more information in this field of investigation, the Dental Institute has engaged in research to evaluate some of the psychosomatic aspects of oral disease. For example, fever blisters (herpes labialis) and canker sores (aphthous stomatitis) are both recurrent painful ulcerations of the mucous tissues of the mouth. A study of these disorders as they occurred in a group of 1,800 students at the University of Pennsylvania has recently been reported by Institute scientists.

Analysis showed that 38 percent of the students had a history of recurrent fever blisters. No sex differences relative to this disorder were noted. On the other hand, a significant sex difference was seen in the 57 percent of females and 52 percent of males that had canker sores. In addition these prevalence levels were considerably above those previously reported in population studies by other investigators. Age, racial background, marital status, school, and class differences were not seen in either disease, and students susceptible to episodes of canker sores experience more frequent recurrences than those susceptible to fever blisters. Of particular interest to investigators was the strong relationship noted between emotional factors and aphthous ulcerations. This was seen in both sexes and appeared to be related to the severity of the disease.

Diet and oral diseases

Dental disorders are international in scope, as they recognize no political, territorial, or national boundaries. Moreover, we know the dental disease profile of the United States reflects only a small fraction of a worldwide pattern of prevalence and severity. Recognizing the need to broaden the scope of studies to include diverse population groups where diet, climate, and cultural habits differ from our own, the Institute has extended its investigative program to selected geographical areas including a number of foreign countries. For example, epidemiologic studies to identify patterns of association between diet and oral disorders have recently been completed in Alaska, Ethiopia, Peru, Ecuador, Chile, Vietnam, and Thailand. This work was done in cooperation with the Interdepartmental Committee on Nutrition for national defense. In general, studies to date of foreign and domestic populations have failed to establish an association of dental decay with a deficiency of any known nutrients. Reports show, for example, that both high and low levels of decay in Alaskan Eskimos were associated with a high intake of protein, moderate intake of fat, low consumption of carbohydrate, and low plasma level of vitamin A. On the other hand equally low, as well as lower decay prevalence levels were seen in Ethiopians living on a comparatively low-protein, high-carbohydrate cereal diet, high in thiamine; and in Vietnamese on a highly milled rice diet, yielding only margial amounts of thiamine and riboflavin. Also unexplained were the large proportions of individuals in each of the groups that were totally free of dental decay.

Where decay levels in these populations were generally low by U.S. standards. the prevalence and severity of periodontal disease were correspondingly high, For example, reports from Ethiopia, Ecuador, and Vietnam showed the levels of periodontal disease were much above any so far recorded for the continental United States. Deviations from this pattern of prevalence were noticed among primitive groups of Alaskan Eskimos and the Ecuadoran Indians, where a reduction in periodontal disease was related to high thiamine excretions and lower levels of plasma vitamin A. Elsewhere in Alaska, and generally in Peru, periodontal disease levels were comparable with those seen in the United States among people of low socioeconomic status.

RESEARCH GRANTS

The support of research in our Nation's dental schools and other institutions has, in the short space of 10 years, established a significant potential for the conquest of oral disease. Many studies begun several years ago are now generating important scientific knowledge, and new programs continue to exemplify the increasing scope of dental research.

For example, noteworthy this year in the field of congenital anomalies was the award of a program grant for studies of the etiology, functional activity, and therapeutic management of a congenital cleft lip and cleft palate syndrome. This dentally oriented research program involves a broad spectrum of investigation ranging from the embryology and genetics involved to an understanding of mechanism, evaluation of treatment, and psychosocial factors. The grant places emphasis on an integrated team approach to the cleft palate problem and, quite importantly, it is also designed to train investigators and practitioners in this complex field of inquiry.

Periodontal disease is of major importance to the oral health field. In an effort to gain a better understanding of this disease, basic studies have been extended by the award of grants to study the biosynthesis of collagen in periodontal tissues. Another significant advance in the study of periodontal disorders is the support of studies on dental calculus. This program grant supports an integrated, multidisciplinary approach to the factors responsible for tartar formation and the development of methods for its prevention and proper removal.

Dental scientists are also interested in the phenomenon of aging as related to oral health, since all living cells, tissues, and organs change progressively with the passage of time. An example of a basic research study with an aging component is the investigation by grantees of the organizational structure and function of mineralized tissue. In order to understand the nature of certain pathological conditions associated with abnormal calcification, basic information on both normal and abnormal mineralization is needed.

In another field, dental grantees are now engaged in studies of various local and systemic factors in an effort to learn more about the onset of pathologic conditions in the mouth. For example, interesting reports have appeared this year on studies of the nervous system as one of the contributing etiological factors in oral disease. Data from some of this work have already shown that irritation of certain areas of the brain stem may effect basic pathologic changes in the oral cavity as well as in the gastrointestinal tract. Thus opened for consideration is the possible role that more subtle neurological disorders may play in the general behavior of dental and related diseases.

These are but a few examples of the type of extramural research currently being supported in broad fields of interest to dentistry. Many other studies are now underway in experimental caries research, electromyographic studies of jaws, dental radiation investigations, and dental public health research, to name but a few.

The history of congressional appropriations to the Institute for research project grants is one of steady growth, and each year since 1950 has witnessed new vigor on the part of the profession to better understand and thus control oral disease. Moreover, those of us in dental research today are convinced that our investigations must be even further extended in the scientific disciplines concerned with the life sciences, for the majority of these are now required for dental research.

RESEARCH TRAINING

The primary objective of our graduate training program is to increase the number of competent researchers and teachers in dental schools and other research institutions. The program is designed to meet the chronic shortage of clinical and basic science personnel now available to these institutions. Further, it has been established that substantial numbers of additional trained personnel will be required to guarantee an increased number of practicing dentists and to perpetuate research at the national level. Moreover, increased physical facilities are being built to accommodate research and at least 10 new dental schools are planned in the next decade. This modest but successful program continues to provide important impetus to the establishment of centers devoted to training outstanding research personnel in dentistry.

The present fellowship and training programs are as yet too young to allow a realistic evaluation of factual accomplishments at this time. However, several meaningful observations are at hand that already suggest a greater emphasis on the training of personnel in research methodology as related to dentistry. A second emerging priority, of course, is that greater effort should be made to further exploit the basic, scientific personnel potential already trained and available outside of the dental schools. Many of these investigators could now be making significant contributions to dentistry.

Recognizing the manpower problem and the opportunity to increase the quality of dental services by the use of ancillary personnel, funds were allocated this year to establish a new program of dental student training grants. The purpose of these is to provide necessary financial assistance to dental schools for establishing, as an integral part of their undergraduate curriculums, formal programs for teaching dental students to work effectively with chairside assistants. The long-range purpose is to help relieve, through a more effective utilization of all existing dental skills, the continuing decline in the supply of dental services. Although these training grants are in the first year of operation, this program is actually the successor to a highly successful experimental project launched in 1956 by what is now the Division of Dental Public Health and Resources. When it became apparent that traininng in the use of chairside assistants could and should be given by all dental schools, the National Advisory Dental Research Council recommended that a portion of our training grant funds be allocated for this purpose. Accordingly, last January each of our 47 schools became eligible for assistance under this program. As this statement was prepared, a total of 37 schools had applied for grants, including 9 schools that were already conducting training programs under the original experimental project.

Last, but certainly not least, the Institute's fellowship program has become virtually indispensable as a means of training research personnel. In addition to the regular fellowships—that is, predoctoral, postdoctoral, and special—considerable use has been made of awards for the postsophomore and the student part-time fellowships. This latter program emerges as perhaps the most singularly valuable grant mechanism for attracting dental graduates to careers in research and teaching. The recent expansion of this type of award to include schools of public health has been very well received. For example, this year in addition to the eight units allotted per dental school, an additional two units were made available to each school of public health. At present, all 47 dental schools have requested the maximum number of units for an aggregate of 370 units. A continuing study of these programs shows that a high percentage of participating students continue their research training by receiving support from the post-sophomore or postdoctoral research fellowships or as trainees under the training grant program. Also, the 1961 budget provided funds for establishing the new career research professorship program designed to provide stable careers for our country's most outstanding dental research workers.

In conclusion, Mr. Chairman, the amended request for the National Institute of Dental Research in 1962 is $13,933,000 as compared with the adjusted appropriation of $13,350,300 for 1961. Due to nonrecurring expenses in 1961, this allowance for 1962 will provide net program increases of: (1) $993,000 for approximately 69 new research projects; (2) $400,000 for the recently initiated chairside assistant program; (3) $500,000 for the regular graduate training program; and (4) $331,000 for direct research. The request for 1962 is distributed among program activities as follows:

Grants:	
Research	$6, 718, 000
Fellowships	760, 000
Training	3, 291, 000
Subtotal, grants	10, 769, 000
Direct operations:	
Research	2, 706, 000
Review and approval of grants	310, 000
Administration	148, 000
Subtotal, direct operations	3, 164, 000
Total 1962 appropriation request	13, 933, 000

Mr. Fogarty. Dr. Arnold, do you have an oral statement you would like to make at this time?

Dr. Arnold. Yes, Mr. Fogarty. I would like to briefly summarize our statement which has been submitted for the record, if it meets with your permission.

Mr. Fogarty. Yes; you may proceed.

Dr. Arnold. First, I do want to make a comment. As you and some of the other members of the committee recognize, our chief dental officer, Dr. Knutson, is usually here with us to testify. I want to assure you that his absence is not because of a lack of interest in our program. He is on a trip of South America to study dental research and dental education in South America and he could not be here with us.

Mr. Chairman and members of the committee, the following statement will review for this committee progress made by the National Institute of Dental Research in the study of oral diseases.

PROGRAM HIGHLIGHTS, 1962

In our studies to assess the cariostatic effects of certain mineral phosphates in animals and in humans that I reported on last year, we had associated dental caries inhibition with a localized reaction that occurs on the exposed surfaces of teeth. In the past year, however, our scientists have found that an organic phosphate compound—sodium phytate—administered via the diet, caused a dramatic reduction in rat caries. Inasmuch as phytate is hydrolyzed primarily in the lower intestine, a cariostatic effect of possible systemic origin is now in evidence. In other studies this year, investigators have observed a strong relationship between certain emotional factors and aphthous stomatitis, a painful recurring ulceration of the mouth. In the field of epidemiology, studies to date of foreign and domestic populations have failed to establish an association of dental decay with a deficiency of any known nutrients. Generally, where decay levels in foreign populations were low by U.S. standards, the prevalence and severity of periodontal disease were correspondingly high.

PROGRAMS TO RECEIVE EMPHASIS IN 1962

Anticipating the occupancy of our new research building in 1962, a section on enzyme chemistry was established this year. Another new program will be concerned with the anatomy and physiology of the mouth and pharyngeal region and with distortions of form and function resulting from congential anomalies or neurological disorders. Studies in experimental embryology and immunology will also receive special programed attention in the near future. The already proven value of the germfree animal in identifying bacteria pathogenic to oral tissues is illustrated in recent findings that suggest dental decay may be caused by a single or only a few specific organisms.

This gives us a lot of hope. If this proves true, the possibility of its eventual control with vaccines or specific chemotherapeutic agents will be greatly enhanced.

RESEARCH AND TRAINING GRANTS

In the area of research project grants a recent evaluation of our program shows that about 80 percent of the available funds are now awarded to research workers in the 47 dental schools. Analysis of this support, viewed in parallel with manpower shortages, serves to emphasize the need for attracting to dental research more investigators in the basic science departments of universities and colleges, hospitals and clinics not directly associated, shall we say, with dental schools themselves. We hope to move forward in this area this year.

Although the expanded horizons of dental research at the Institute and in many dental schools suggest an increasing availability of well-trained scientists, the facts are that dentistry, like most health professions, is party to a mounting competition for scarce professional manpower. Therefore, in 1962 we will look with a sense of great urgency to our fellowships and training grants as the best means of sponsoring advanced study and establishing graduate training centers at dental schools, hospitals, and other institutions.

SUMMARY OF 1962 BUDGET

In conclusion, Mr. Chairman, the amended request for the National Institute of Dental Research in 1962 is $13,933,000 as compared with the adjusted appropriation of $13,350,300 for 1961. Due to nonrecurring expenses such as equipment for the new building and so forth in 1961, this allowance for 1962 will provide net program increases of: (1) $993,000 for approximately 69 new research projects; (2) $400,000 for the recently initiated chairside assistant program; (3) $500,000 for the regular graduate training program; and (4)

$331,000 for direct research. The request for 1962 is distributed among program activities as follows:

Grants:	
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Administration	148, 000
Subtotal, direct operations	3, 164, 000
Total 1962 appropriation request	13, 933, 000

I think this, Mr. Chairman, summarizes briefly our opening statement and our program aims. I will be very happy to answer any questions that you or the committee may desire.

Mr. FOGARTY. All right, Dr. Arnold.

1962 BUDGET

The appropriation for 1961 is $15.5 million but the sum of $2,149,700 is proposed for transfer to the Bureau of State Services, leaving $13,350,300.

The Eisenhower budget is for $13,035,000 for 1962, or a reduction of $315,000.

Dr. ARNOLD. That is correct.

Mr. FOGARTY. You had a reduction of over $300,000?

Dr. ARNOLD. As I explained, Mr. Chairman, yes, it is, moneywise, a reduction. If you will recall, however, there was some $800,000 in nonrecurring items in our 1961 budget.

Mr. FOGARTY. The budget amendment increases the request to $13,933,000, or an increase of $582,700 over 1961?

Dr. ARNOLD. That is correct.

Mr. FOGARTY. This is the smallest budget amendment of any of the Institutes; is that right?

Have the "powers to be" got something against dentistry?

Dr. ARNOLD. Mr. Chairman, we are the smallest of the Institutes out there.

Mr. FOGARTY. It is by far the smallest increase, too.

Dr. ARNOLD. I do feel, Mr. Chairman, that the amended budget is a very progressive budget, and I do feel——

Mr. FOGARTY. You do not believe you are being discriminated against?

Dr. ARNOLD. I do not; no, sir.

Mr. FOGARTY. For what amount did you ask the Department?

Mr. SEGGEL. $17,915,000.

Mr. FOGARTY. $17 million? Well, you were cut to the extent of $4 million?

Dr. ARNOLD. It was $16 million. May I correct the record?

Mr. FOGARTY. $16 million?

Dr. ARNOLD. The NIH asked the Department for $16,923,000.

Mr. FOGARTY. Well, that represents a cut of $3 million. Let us get the record straight.

Mr. SEGGEL. The original request by the Dental Institute to the NIH was $17,915,000.

Mr. FOGARTY. Well, you really got cut. You got cut more in proportion than any other Institute, then. You not only got the smallest increase of any Institute, but you got cut more than any other Institute, percentagewise.

Dr. ARNOLD. I do not know what the percentage of the cut is, Mr. Fogarty.

Mr. FOGARTY. I am just taking it from these figures, and that is why I asked you if you are being discriminated against.

Do you still think you could use that $17 million that you asked for?

Dr. ARNOLD. I am sure we could, and use it effectively, Mr. Fogarty.

Mr. FOGARTY. All right; will you supply to us, as all the other Institutes have, what you originally asked for, and give us a breakdown of how you would use that additional $4 million, if it were given to you?

Dr. ARNOLD. I shall do that, sir.

(The matter referred to follows:)

Development of 1962 budget estimates for National Institute of Dental Research

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revised submission to Bureau of Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$7, 843	+$179	$8, 022	−$504	$7, 518	−$1, 580	$5, 938	$7, 318	$600	$6, 718
Fellowships	1, 300	−430	870	0	870	−110	760	870	110	760
Training	5, 500	−609	4, 891	−1, 600	3, 291	0	3, 291	3, 291	0	3, 291
State control programs	0	0	0	0	0	0	0	0	0	0
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	14, 643	−860	13, 783	−2, 104	11, 679	−1, 690	9, 989	11, 479	710	10, 769
Direct operations:										
Research	2, 777	−57	2, 720	−24	2, 696	−68	2, 628	2, 706	0	2, 706
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	335	−58	277	+5	282	−5	277	348	38	310
Training activities	0	0	0	0	0	0	0	0	0	0
Professional and technical assistance	0	0	0	0	0	0	0	0	0	0
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	160	−17	143	0	143	−2	141	148	0	148
Total direct operations	3, 272	−132	3, 140	−19	3, 121	−75	3, 046	3, 202	38	3, 164
Total obligations	17, 915	−992	16, 923	−2, 123	14, 800	−1, 765	13, 035	14, 631	748	13, 933

1962 original request

Activities	*Amount*
Grants:	
Research	$7, 843, 000
Fellowships	1, 300, 000
Training	5, 500, 000
Total grants	14, 643, 000
Direct operations:	
Research	2, 777, 000
Review and approval of grants	335, 000
Administration	160, 000
Total direct operations	3, 272, 000
Total estimate	17, 915, 000

The increase of $3,982,000 over the revised estimate would be used as follows:

Grants:	
Research	+$1, 125, 000
Fellowships	+540, 000
Training	+2, 209, 000
Total grants	+3, 874, 000
Direct operations:	
Research	+71, 000
Review and approval of grants	+25, 000
Administration	+12, 000
Total direct operations	+108, 000
Total increase	+3, 982, 000

ADEQUACY OF 1962 BUDGET FOR RESEARCH GRANTS

Mr. Fogarty. Do you think the budget before us will permit you to finance all of the approvable applications for research grants which you will receive in 1962?

Dr. Arnold. In terms of information we have had in the last go-round of our Council, we will have no backlog from 1961, carrying into 1962.

I do feel, however, that the budget we have—that is the 1962 revised budget—may not permit us to support all of the anticipated approved projects.

CONSOLIDATION OF DENTAL PUBLIC HEALTH AND RESOURCES ACTIVITIES

Mr. Fogarty. Last year our committee suggested consolidation of all dental public health and dental resources activities in one place, with the result that these are now consolidated in the Bureau of State Services.

Do you think this has been a good move?

Dr. Arnold. I do, Mr. Fogarty. I think the committee was very wise in making the suggestion, and I assure you that we are in full cooperation with the activities transferred down there.

ADVISABILITY OF LIKE CONSOLIDATIONS ELSEWHERE

Mr. Fogarty. Why is it good for the Dental Institute and not good for any other institute, Dr. Shannon?

Dr. Shannon. I do not think there is any quarrel administratively with the way the dental activities are handled, out of a single focus downtown, because that is precisely the way other activities that are spread between other services are handled, and this particularly pertains to Heart and Cancer. Those functions that go to the Bureau of State Services for execution go to a single accounting point and a single administrative organization. So, this would be in line with the organizational structure of the Heart and the Cancer Institutes. The problem in the past has been that these were not budgeted within a single downtown organization, nor were all the funds expended downtown budgeted in a single lump sum. There were two different provisions: One related to dental practice and the other related to dental resources. In addition, certain of the dental technical assistance programs appeared in the section of the budget which appeared to be expended at the Bethesda accounting point. What this does is to bring the three items together in a single accounting point for a single program development.

Mr. Fogarty. But you have not done that with respect to the other Institutes?

Dr. Shannon. But this already obtains in the other Institutes, Mr. Chairman.

Mr. Fogarty. Not in your budget.

Dr. Shannon. It does, in fact, sir; yes, sir.

Mr. Fogarty. I thought the Surgeon General told us differently.

Mr. Kelly. I think they are developed somewhat differently. I think what we have done in this budget we have before you is make the dental resources program more nearly comparable to the way we have financed the nursing resources program. I think there is some degree of comparability which can be made also with the venereal disease program and the tuberculosis program. But, I think it is true that although we have made a series of fairly significant adjustments in the way of funding the Public Health Service in the 1962 budget, we do not go so far as to transfer to the Bureau of State Services the funding of the control grants to States and the technical assistance programs in the National Institutes of Health which are, in fact, administered by the Bureau of State Services. It could be argued that we should do so, but as yet, we have not recommended it.

Dr. Shannon. Operationally they are pulled together under a single accounting point within the Bureau of State Services.

Mr. Fogarty. Is there any substantial difference, then, between that operation and the Dental Institute?

Mr. Kelly. I think, as I would view it, we took the entire Bureau of State Services operation and funded it in the Bureau of State Services. The activities carried out by the Bureau of State Services with funds appropriated to NIH in connection with Heart, Cancer, and Mental Health are not really the total programs carried under the Bureau of State Services, but they are a portion of them. I think there is some distinction between the two. While I think you can argue with some consistency on it——

PROPOSED CHANGES IN PHS APPROPRIATION STRUCTURE

Mr. Fogarty. Do we have at one place in the record the changes that you have made from last year's budget structure for PHS and all of these transfers?

Mr. KELLY. I believe so; yes, sir.

Mr. FOGARTY. I hope all the work you went to regarding changing the structure was not a lot of work that was wasted.

Mr. KELLY. I might add, Mr. Chairman, that we not only did this because we thought it was an advisable thing to do, but we think the way we presented it for your consideration this year makes a big improvement in the administration of funds; and that with limited exceptions we now have the funding for each of the major organizational units programed so that there is a single appropriation with respect to those working units. We thought we were making this worthwhile change in response to the recommendations of this committee, both in respect to environmental health and with respect to dental resources.

Mr. FOGARTY. You would not be surprised if I disagreed with you, would you, when we mark up this bill?

The Bureau of the Budget had quite a bit to do with it, did it not?

Mr. KELLY. In terms of consolidation of appropriations they did, but in terms of the transfers, these were our recommendations and I must honestly say, from your report, I thought they were yours, too.

Mr. FOGARTY. You are talking about transfers and not the consolidation?

Mr. KELLY. Not consolidation; that is right.

Mr. FOGARTY. From what I have seen so for, I have no quarrel with the transfers.

MULTIDISCIPLINARY GRANT PROGRAM

What is this multidisciplinary grant program into which you are getting, Doctor?

Dr. ARNOLD. I will give you a concrete example of what we are trying to do, Mr. Chairman. We feel that both in periodontal disease research and in the field of cleft palate research, we must go into broader types of project grants. I have heard them described as program grants and so forth. Take the cleft palate problem, for example: In order to do research in the field of cleft palate, we need the plastic surgeon, the orthodontist, the prosthodontist, the speech therapist, and others together with the ordinary dentist who takes care of just the cavities and fillings that develop in the mouth. We are trying to develop some teams throughout the country, on the advice of our Council, to do this very thing.

Mr. FOGARTY. Would that be similar to an institutional grant?

Dr. ARNOLD. I do not think so; no, sir. I think it is more similar to the multidisciplinary types of grants which are, shall we say, like the center grants.

Dr. SHANNON. It is similar to a straightforward research grant.

Mr. FOGARTY. It is something like an institutional grant, is it not?

Dr. SHANNON. No, sir; it is for a specific project of work, definable as such, where there is a principal investigator and he has associated with him leaders in collateral fields who together do a different type of research that cannot be done independently. This is presented as a project in precisely the same way as the so-called straight research grants, but it is a more complex project. The institution, as such, does not participate in the development of the grant, nor does it benefit in terms of dollars.

Mr. FOGARTY. Does this grant go through the same process of the Study Section and Advisory Council?

Dr. SHANNON. Yes, sir.

INCREASE IN TRAINING GRANTS

Mr. FOGARTY. You do have a small increase in training grants in your budget, do you not?

Dr. ARNOLD. That is correct, sir. We do have an increase in the amended budget of $326,000, which in 1962 would bring the total to $3,291,000.

Mr. FOGARTY. At page 215 of the justifications, in connection with training grants, you say the primary objective is to increase the number of people "who desire to pursue academic dental teaching and dental research careers."

What do you mean by that?

Dr. ARNOLD. Well, I think one of our problems, Mr. Chairman, is that we are faced with the same manpower shortage in dental research as faces the total medical research picture. In my own opinion, speaking now from the dental standpoint, I think we have quite a difficult job in getting qualified, trained people. We are trying to aim our program at producing an academic man or research man. Unfortunately, it was only a few years ago that, percentagewise, we had less than 2 percent of our graduates coming out of dental schools who went on into academic and research careers. I think, although we have not calculated the latest figures, you have some 13 to 15 percent of medical school graduates that go into adacemic and research careers. We are trying to encourage this by the use of training grants to the dental schools and other institutions.

Mr. FOGARTY. Is this anything different than the other Institutes' programs?

Dr. ARNOLD. Not to the best of my knowledge. We have confined our program—our training grant program—to this purpose. It has two aspects to it. One is the training at a graduate level of individuals from dental schools or other institutions in terms of postdoctorate graduate training.

Mr. FOGARTY. Do you have any idea how many of these people stay in research?

Dr. ARNOLD. I cannot answer you specifically on this. We did not have very much money in this area until some 3 years ago when we started our training program. I am happy to report that at one or two of the places—because it takes about 3 years to produce this product—we have been able to check this point and we are very pleased. I can report to you that in the range of 90 percent of those we can check on today are in part-time or full-time research or academic positions after coming out of this program.

Mr. FOGARTY. Did you want to say something in addition to this, Dr. Shannon?

This entire field of training is a real problem in this entire budget, and I have been finding fault with the fact that there are few increases for training and fellowships throughout the budget.

Dr. SHANNON. I did not want to comment on the dollar value of the budget, Mr. Fogarty, but rather to emphasize——

GENERAL POLICY REGARDING BUDGET FOR TRAINING

Mr. Fogarty. Do you want to comment on the policy with respect to almost no increases in these areas?

Dr. Shannon Well, there are actually increases in Dr. Arnold's budget and, percentagewise, in the training area they are substantial. In fact, this was one of the areas that we highlighted. While, in general, we held back training last year, we permitted Dental to go ahead——

Mr. Fogarty. I thought Dr. Felix estimated the other day that he could effectively use several millions of dollars more in training, if he had it, but that he did not get very far with his budget.

Dr. Shannon. I think that Dr. Felix's budget is quite different from the Dental budget. The primary decision that the Institute of Mental Health must make, at this point in time, with policy guidance from the executive branch and from the Congress, is the extent to which they need to develop training programs, because, really, they have the primary responsibility for the practical training of psychiatrists and psychiatric personnel. I think this is quite a different decision from that presented by the budget of the Dental Institute; which is, primarily trying to make up a critical shortage of research personnel for its program.

Now, as an example, the absence of scientific research personnel will lead the Dental Institute this year to have a balance in the grant area, even in the absence of, well——

Mr. Fogarty. How much of a balance?

Dr. Shannon. I do not know the figure. What will the balance be?

Dr. Arnold. In the range of $500,000.

Dr. Shannon. This is a very substantial sum. It means that despite the importance of the problems they are faced with, they have not had an adequate number of approved research grant applications to utilize the funds which the Congress made available. This stems in no small measure from the past history of dental research in this country. That is now being overcome, but, traditionally, there were only a few adequate facilities for dental research in the institutions for dental education in this country. There was an absence of long-term support for the research programs and there was a dearth, if not a complete absence, of grants for research in dental institutions of higher education. Even today, only a portion of our dental schools can provide these three things; namely, adequate facilities, long-term support and grants for research.

The importance of this is emphasized by the fact that dental research is not of the character that has led to the establishment of many independent dental research activities. So we are essentially totally dependent for the development of a dental research program on our educational institutions. They are all crowded and suffer all of the limitations of our medical schools in terms of resources and facilities for educational programs. I would say they are even in worse shape than our medical educational institutions to provide a strong base for dental research.

It was for this reason that we felt that it was realistic, if on the conservative side, to encourage the Dental Institute to go forward with at least a part of its training program in the budget.

I would point out that the field of dental research has a tendency to become highly specific and highly applied, unless, as Dr. Arnold's budget proposes, one emphasizes to our dental schools that we are interested in establishing a rather broad base for their applied studies. This is the significance of these so-called multidisciplinary grants, which bring together the physiologists, the pathologists, the psychologists and bring the electron microscope and the more powerful tools of science that have evolved in the past year to bear on these very pressing dental problems. But, Mr. Fogarty, I think that this area will continue to evolve more slowly than any of the other areas, because of the two things I pointed out—the complete dependence of the program on the institutions of higher learning and the very difficult financial situation that these institutions find themselves in.

Mr. Fogarty. Would not this help their financial problem?

Dr. Shannon. No, Mr. Fogarty because they are lacking in space and they are lacking in career positions. They do not have the faculty depth that is required.

Mr. Fogarty. I am not talking about just dental research, but I am talking about all of the Institutes of Health.

Dr. Shannon. Well, I do not quite understand the question, Mr. Fogarty.

Mr. Fogarty. I thought you said they have a problem financially—these schools of higher learning?

Dr. Shannon. Yes, but I am pointing out that——

Mr. Fogarty. Would not this help them if our training program all along the line was stepped up?

Dr. Shannon. I think it will help the men in the other schools of higher learning more than in the dental schools, because it is my personal belief that the space problem and the faculty problem in dental schools is much more critical than those in the medical schools.

Mr. Fogarty. Let us get away from the dental schools.

We have a shortage of trained personnel in the medical profession and also in all these other allied groups like radiological health and environmental health. Do you not think it would be a good idea to push this training program a little? Would it not only help close the gap between what we have now and what is needed but also help these schools of higher learning at the same time?

What is the level of the budget for training now?

Dr. Shannon. It is around $120 million.

Mr. Kelly. It is about $120 million including training grants and research fellowships.

Mr. Seggel. $96 million for training grants and $22 million for fellowships.

Mr. Fogarty. We want you to tell this committee what you think—what your personal convictions are.

Dr. Shannon. My own conviction is that until we can break what is still a serious bottleneck in facilities and until we can provide more stable careers in research, either directly or through institutional grants, I personally believe we have got to the point where we will not, in the long run, enhance our research base much beyond what it is today without a change in the mechanics whereby we make funds available.

Mr. Fogarty. With the existing authority that we have today, what can we do?

Dr. SHANNON. If we can be assured of a stable program for supporting careers in science—of which research is the beginning—if we were assured of stable support by the institutional research grants, then, I think, we have a base for substantial expansion of the training program.

Mr. FOGARTY. That might be a hard thing to guarantee.

Dr. SHANNON. I do not mean guarantee, sir.

Mr. FOGARTY. But, Congress, in effect, has been giving that guarantee in the last 10 years, has it not?

Dr. SHANNON. Yes, sir. But, Mr. Fogarty, I do not mean the guarantee. If in your report, regardless of what is done this year—and this year is mostly over—the committee declared that they would support the concept of providing institutional stability by the provision of institutional research grants and if you said that this is highly advisable and should be looked into and should make the best progress it can, then I think we would have the basis for the expenditure of further funds in training.

Mr. FOGARTY. How much do you think we should appropriate next year?

Dr. SHANNON. Mr. Fogarty, I could not give you a figure for that. I just have had the professional judgment estimates of the Institutes since this morning and, this, I would have to look at.

Mr. FOGARTY. Will you supply that for the record?

Dr. SHANNON. Yes, sir, I would be glad to.

(The information requested follows:)

The professional judgment budgets prepared by the Institutes include a total training grant level of $139,638,000. Proposals at this level undoubtedly reflect a genuine need for educational aid and greater support of academic career positions which would expand and strengthen institutional faculties. I believe much of this need can be better met by general aid to professional education and the promotion of career stability through such means as the institutional research grants.

FLUORIDATION

MUNICIPAL FLUORIDATION

Mr. FOGARTY. Dr. Arnold, are you satisfied with the progress in fluoridation of municipal water supplies?

Dr. ARNOLD. No, I am not, Mr. Fogerty. I cannot explain to you the answer, but I am sure you and the rest of the committee recognize that we have not progressed as well as we feel we should have progressed in this field.

I think there are, as either I or Dr. Knutson testified before this committee last year, methods of improvement. We have done quite well in the larger communities, but we are down to the smaller communities and we have not progressed as we would like to see it progress.

When one figures that the use of fluoridation of water supplies for the control of dental caries is in the range of 10 years old; that is, as a recommendation from not only the Public Health Service, but from the American Dental Association and others, he is discouraged. Based upon the last figures I saw, we had some 1,950 or 1,980 communities and some 37 million people using fluoridated water, but when one looks over the results of the recent referenda that were held, it was defeated 3 or 4 to 1. So, we are not progressing as much as I would like to see.

HOME FLUORIDATION

Mr. Fogarty. Will you tell us the progress, if any, in the development of home fluoridators?

Dr. Arnold. We have made progress in that field. It is not a direct operation of our Institute. It is an operation that is administratively carried on the Division of Dental Public Health and Resources. We do have what can be considered practical home fluoridators where a person, shall we say, has a well and he would hook the fluoridator into his own personal water supply. It is not practical in comparison to municipal fluoridation because it is more expensive and requires continual inspection and upkeep.

Mr. Fogarty. What about fluoride tablets? Are they being used to any extent?

Dr. Arnold. To no great extent, Mr. Fogarty. We did report a study this past year that we had under operation some 15 years. In fact, it started because I started feeding my own children tablets back before fluoridation was actually recommended and endorsed.

This group was developed from professional people in the Public Health Service, and all who wanted to do something about feeding their children fluoride. We did furnish them fluoride tablets, we did keep records on them. The results have been very favorable.

Again, from a practical standpoint, you are depending on an individual to give a daily dose for 8 to 10 years; and out of the some 350 or 400 professional families who asked for the tablets and started this procedure, as I recall the figures we had 120 children, we could even have 6 or 8 years or more of recorded experience for the study. It is not practical from that standpoint.

Dr. Shannon. May I ask a question, Mr. Fogarty?

Mr. Fogarty. Yes.

Dr. Shannon. I don't want to disclose my ignorance for the record, but it occurs to me that the fluoride ion is a type of ion that can probably be given once a week rather than every day to accomplish the same effect. This is not an ion that is rejected rapidly in small quantities, is it? I do not want to get involved in this.

Dr. Arnold. I will answer that this is a possibility, but it (fluoride ion) differs in comparison with vitamin supplements, and so forth. We do not know whether this could be true.

Another area where they are working on the fluoride tablet program to the greatest extent, I think, is in Switzerland. They are using it as a school health program where the schoolchildren are given a tablet a day under supervision. This has to be used under supervision or prescription. The results there are very favorable but they do not compare, percentagewise, as favorable as water fluoridation because the children do not start this until they are 5 or 6 or 7 years of age.

There is a potential of doing this in rural areas, and we now have such programs under consideration. I am hoping that studies of this sort will be in operation in this country before too long.

Mr. Fogarty. Mr. Denton?

Mr. Denton. No questions.

Mr. FOGARTY. Do you have anything else you want to say?
Dr. ARNOLD. No.

INCIDENCE AND COST OF DENTAL DISEASES

Mr. FOGARTY. We will place in the record at this point your statements on the incidence and cost of dental disease and the highlights of your research.

(The statements referred to follow:)

NATIONAL INSTITUTE OF DENTAL RESEARCH

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases dealt with in the Dental Institute, and the estimated annual cost to the Nation.

1. DEATHS RELATED TO DENTAL DISEASE

No information available.

2. DISABILITIES CAUSED BY DENTAL DISEASES

Oral diseases are among the most prevalent of all diseases of mankind. Dental caries affects 95 percent of the population of the United States, and more than 90 percent of children of school age. One child in ten has some form of malocclusion, and 1 in 800 is born with cleft lip or palate. Periodontal disease is the main cause of tooth loss in adults. The treatment of oral diseases places a heavy burden on our population, with dental care costing one of every six dollars spent for health services.

3. ESTIMATED ANNUAL COST TO THE NATION

More than 160 million people in the United States either have been victims or face the almost certain prospect of suffering from one or more dental diseases. Dental disorders are progressive, cumulative, and require many hours of scarce professional treatment time. Family expenditures for treatment services total $2 billion annually, or 15 cents out of every dollar spent for personal health services. The public health problem of dental disease is complicated by a declining proportion of dentists to population, cost of treatment, and a lack of public understanding of oral health problems.

HIGHLIGHTS OF PROGRESS IN DENTAL RESEARCH, 1960

Items of interest on program developments and research studies conducted and supported by the National Institute of Dental Research

DENTAL CARIES

Mechanism of dental decay studied in gnotobiotic animals

Previous studies at the University of Notre Dame using germfree rats fed a cariogenic diet provided dental scientists for the first time with unequivocal evidence that experimental caries do not occur in the absence of bacteria. Following this discovery attention was logically directed toward isolating specific decay producing micro-organisms in gnotobiotic animals. These studies soon led to the establishment of a direct cause and effect relationship between dental decay and an enterococcus (reported from Lobound) and a single strain of oral streptococcus reported by NIDR scientists.

In studies this year by Drs. Robert J. Fitzgerald and Harold V. Jordan, Laboratory of Microbiology, and Dr. Harold R. Stanley, Clinical Investigations Branch, 16 weanling white rats of the Lobound germfree strain were divided into two groups and housed in Reyniers' germfree tanks. Animals in group I were monoinfected with a streptococcus isolated from the oral cavity of a caries-active rat, while those in group II remained as germfree controls. A third group of rats used as conventional controls were offspring from breeders of the Lobound germfree strain, brought to a conventional environment prior to mating. Animals in all three groups were maintained on the same cariogenic diet that was autoclaved and supplemented with vitamins.

Each of the rats in the conventional control group, sacrificed after 100 days on the cariogenic diet, and all animals in the monoinfected group, sacrificed after 77 days, showed extensive cavitation frequently involving both the dentine and pulp chamber of molars. In contrast, the teeth of the germfree animals, sacrificed after 84 days, were free of caries in spite of considerable food impaction and occasional fracture of a molar cusp.

These significant studies with gnotobiotic animals have extended the knowledge of oral disease by demonstrating the etiological role of the streptococcus organism in the production of experimental caries.

Dental scientists seek caries inhibiting agents

As previously mentioned germfree animals have clearly established a causal relationship between certain oral bacteria and dental caries. While antibiotics are effective in depressing the oral flora, certain undesirable features such as sensitivity, and development of antibiotic resistant organisms limit their practical use. On the other hand, chemical agents which interrupt or alter the metabolism of oral bacteria may provide a rational approach to the problem. Thus, investigators in the Laboratory of Microbiology reported this year on experimental studies with carbonyl-binding compounds as examples of potentially useful agents.

Sodium metabisulfite, a carbonyl-binding agent, has been shown to inhibit experimental caries in rats. Two other carbonyl-binding agents, CMA (carboxylmethoxylamine hemihydrochloride) and dimedone were also tested and found active. In studies conducted by Drs. H. V. Jordan, R. J. Fitzgerald, and Miss N. D. Berger, these three compounds were tested separately in laboratory rats maintained on a cariogenic diet. Results showed that an 82 percent reduction in caries score was obtained when CMA was fed in the diet at a level of 0.004 molar for the first week and 0.002 molar for the remainder of the 90-day test period. Feeding of 0.016 molar sodium metabisulfite resulted in an inhibition of 86 percent, while rats fed the aldehyde-binding agent dimedone at a level of 0.029 molar showed a 55 percent reduction in caries score. *In vitro* experiments showed that the relative cariostatic effects of these three compounds generally paralleled their growth-inhibiting properties for a variety of micro-organisms including lactobacilli, streptococci, staphylococci and diptheroids.

These continuing studies of inhibiting agents, coupled with recent contributions defining the production and transmission of caries, and the identification of specific oral pathogens, are providing valuable new information necessary for a practical approach to the prevention and control of dental decay.

New method for the assessment of cariostatic agents

The screening of potential caries-inhibitory agents in experimental animals is an important prerequisite to clinical trials in humans. Recent progress in studies of the production and transmission of dental caries in hamsters has led to the development of new and improved procedures for the rapid assessment of caries-inhibiting agents in animals.

Conventional screening methods for assessing cariostatic agents are unsatisfactory in that they are limited to the recording of caries initiation and progression of lesions. In demonstrating a new method to assess cariostatic agents, Dr. Paul H. Keyes, Laboratory of Histology and Pathology, selected young albino hamsters known to be infected with a cariogenic flora and maintained them on a caries-test diet for a period of 10–14 days. At the end of this time carious lesions were detectable in the first and second molars; the third molars not yet being erupted. Following this evidence of caries activity, the agent to be tested for cariostatic properties was introduced to the animal via the diet or drinking water. The caries-inhibiting effect of the drug was then determined by noting the degree of arrest of the previously induced lesions in the first and second molars and the degree of prevention of caries in the newly erupted third molars. Finally, withdrawal effects of the agent could be determined by observing the reactivation of caries in arrested lesions and the initiation of new cavities in the previously protected third molars. In the described assessment procedure parallel observations on untreated control animals maintained on the caries producing diet but not receiving any caries-inhibiting agent, showed a rapid progression to severe caries within the test period of 42 days.

Collaborative efforts are now underway with Dr. R. J. Fitzgerald, Laboratory of Microbiology, to trace these events microbiologically. Further studies may delineate more clearly the basic mechanisms involved in the pathogenesis of dental caries.

Investigators study mode of cariostatic action of tetracycline

Previous studies with tetracycline have shown a characteristic deposition of this antibiotic in the bones and teeth of animals. Moreover, caries inhibition has been achieved by the addition of tetracycline to the diets of test animals. NIDR scientists have now reported on studies to investigate the possible relationship between skeletal deposition and residual cariostatic effects. In laboratory experiments by Drs. I. Zipkin and Rachel Larson, Laboratory of Biochemistry, Sprague-Dawley rats were bred and subsequently divided into four groups. Animals in groups A, B, and C received 2.5 mg./ml. of tetracycline hydrochloride in drinking water, and group D received distilled water. Group A animals received the antibiotic during gestation only; group B during gestation and for 14 days following birth; and group C during gestation, lactation, and the remainder of the preweaning period. Group D animals received distilled water until weaning at 21 days of age. A standard laboratory diet was available during gestation and lactation and a noncariogenic diet was offered thereafter until weaning. After weaning, the offspring of animals in all four groups received distilled water and a caries test diet for 60 days.

Tetracycline did not adversely affect litter production, weight gains, diet intakes or fluid consumption in either mothers or offspring. The most striking effect of tetracycline was seen in the marked reduction in caries activity under all experimental regimens. For example, the caries scores for offspring in the three experimental groups were 2.3, 4.5, and 1.8, respectively, and in the control group was 20.3. Although characteristic fluorescence was seen in the teeth and bones, thereby indicating the presence of tetracycline, the low level of caries activity could not be related directly to the incorporation of the antibiotic in the teeth. Rather, tetracycline appears to act by depressing the intestinal microflora and oral flora which had previously been demonstrated by NIDR scientists to contain the caries activating organisms.

Phosphate-dental caries studies focus attention on the chemical reactivity of tooth surfaces

There has been accumulated in recent years convincing evidence that dental decay in experimental animals is dramatically reduced by adding certain mineral phosphates to the diet. This finding provided a firm foundation for clinical studies now underway to assess the inhibitory effects of dicalcium phosphate on human caries. Concurrent with these laboratory and field trials are studies by Dr. F. J. McClure, Chief, Laboratory of Biochemistry, to identify the mode of inhibitory action associated with mineral phosphates.

Dr. McClure has reported evidence that cariostatic effects of the phosphate minerals occur primarily within the oral cavity rather than via an indirect systemic route. For example, it was shown that the relative solubility of phosphates is an important factor; i.e., highly insoluble forms, particularly sodium and ammonium phosphate, are extremely effective. Further support of this hypothesis was seen when insoluble dicalcium phosphate proved to be effective only if sodium chloride was present in the diet to serve as a solubilizing agent. In addition, when Na_2HPO_4 was intubated, thereby bypassing the oral cavity, it was not as cariostatic as when consumed as part of the diet. Just how the cariostatic effects of the phosphate minerals occur remain speculative. However, data gathered to date suggest a direct action of the mineral on oral enamel surfaces thereby focusing attention on the chemical reactivity of tooth surfaces. Paralleling these considerations is the nutrition of the oral flora and their metabolic products which may undergo significant change in the presence of freely available phosphate ions.

Grantees demonstrate chemical activity of succinic acid in enamel decalcification

Lactic acid has traditionally been suspected as the chief causative agent in demineralization leading to dental caries. NIDR grantees reported this year on in vitro studies which showed that, in concentrations found in the mouth, succinic acid is significantly more active than lactic acid in the dissolution of enamel.

In investigations by Mr. W. Wynn, Dr. J. Haldi, and Miss Law, 60 caries free human teeth were extracted, cleaned and the roots covered with acrylic leaving only the enamel surfaces exposed. In order to compare the chemical activity of lactic and succinic acids, 10 teeth were suspended in each of 6 beakers and covered with 250 ml. of one of 6 different solutions. The first three solutions were each 0.1 percent lactic acid, buffered with dilute sodium hydroxide to pH 4, 5, and 6, respectively. The remaining three solutions were 0.1 percent succinic acid, also buffered to pH 4, 5, and 6 with dilute sodium hydroxide. The beakers were then incubated at 37° C. Every 24 hours the solutions were renewed.

Each day a quantity of solution was removed and saved until at the end of 2 weeks, 3.5 liters of each of the six had been collected. The six collections were then evaporated, residues reduced to ash, and analyzed for calcium, phosphorus, and magnesium.

Results showed succinic acid to be considerably more active than lactic acid in removing calcium, phosphorus, and magnesium. For example, at pH 5 succinic removed 24 mg. Ca, 11.5 mg. P and 320 mg. of Mg as compared with lactic which removed 7 mg. Ca, 3 mg. P and 15 mg. Mg. Thus, in this pH range succinic removed approximately 5 times as much Ca and P as lactic acid and up to 20 times as much Mg.

These studies have encouraged further investigations of the origin of succinic acid and other Krebs cycle acids in saliva and their role in in vivo enamel decalcification.

PERIODONTAL DISEASE

Tartar formation not dependent on micro-organism

Previous studies at NIDR have demonstrated the presence of tartarlike deposits in germfree mice. This observation was recently confirmed in studies which showed, with X-ray diffraction analyses, that the crystalline component of tartar formed on the molar teeth of germfree rats was identical to that seen in conventional animals and in humans.

In experiments by Dr. R. J. Fitzgerald, Laboratory of Microbiology, and Mr. E. G. McDaniel, National Institute of Arthritis and Metabolic Diseases, six rats of the Lobund strain were maintained in a germfree environment for 90 days. Periodic bacteriological checks on the food and excreta of the animals confirmed the absence of viable micro-organisms during the test period. At termination of the experiment the animals were sacrificed and a quantity of tartar like material from first molars was collected and pooled for X-ray diffraction studies. The presence of crystalline apatite was detected and, thus, the mineral portion of the germfree calculus was shown to be the same as that in calculus from conventional animals and from humans.

In demonstrating that the formation of typical calculus does not depend on the presence of living or dead micro-organisms, these studies have further explained earlier findings by NIDR scientists that calculus will develop in conventional rats whose oral flora was depressed by antibiotics.

Oral effects of antibiotics are studied

One of the continuing research programs of the Dental Institute is concerned with the testing of antibiotics and other agents which may be used for the control of calculus formation, caries, and other oral conditions.

Scientists have recently completed studies in which chloramphenicol and chlortetracycline, both broad spectrum antibiotics, were tested for their effect on the development of dental calculus and caries in rats. The drugs were added at a level of 0.005 percent to one diet known to promote caries development and to another diet known to accelerate calculus deposition. Calculus severity ratings were then compared with control groups receiving the same diets without antibiotics. The results indicated that neither antibiotic influenced calculus formation. Both, however, demonstrated significant caries reduction in the test animals, with chlortetracycline showing the more marked effect. These results complement the earlier NIDR findings with germfree animals which showed that calculus-like deposits may occur in the absence of oral bacterial while dental decay does not. In the current study further significant findings were made when samples of the crude and ashed calculus deposits from the animals were analyzed and subjected to electron and X-ray diffraction. The mineral phase was identified as hydroxyapatite; thus, the dental deposits in the rat may be considered analogous to oral calculus of humans.

Data from this cooperative study by Drs. R. J. Fitzgerald, H. V. Jordan, D. B. Scott, and Mr. H. G. McCann, representing three laboratories of the NIDR, will provide research workers with a useful tool for the study of deposition and control of dental calculus under experimental conditions

Grantees investigate calculus morphology

Dental calculus and the mechanism involved in its formation are matters of widespread interest because of their combined role in periodontal disease and because of the similarity of calculus to kidney stones, teeth, and bone. Two dental grantees at Harvard University reported this year on electron microscope studies of calculus and some of the factors involved in its development.

Dr. F. Gonzales, senior research fellow, National Institutes of Health, and Dr. R. F. Sognnaes, formerly professor of oral pathology, Harvard School of Dental Medicine, studied microthin calculus sections using electron microscopy and electron diffraction. The resulting micrographs showed occurrence of two types of calcification fronts—one apparently representing an older and more mature concretion—the other showing actively growing and incompletely mineralized early calculus.

Throughout the mass were found the microorganisms typically seen in calculus. Some organisms were completely entombed within solidly calcified areas and were seen in various stages of degeneration. In addition, mineral crystals were observed in the regions between organisms, in the spaces occupied by degenerated bacteria and within some bacteria themselves. Many of these inorganic crystals were of the same size and shape as those in bone. While microorganisms have previously been implicated in calculus formation, these observations graphically indicate for the first time that oral bacteria may themselves be subject to mineral deposition. Continuation studies in this field are designed to explore calculus formation and deal with the developmental stages of the calcification phenomena, as well as histochemical analyses of the substancies involved.

Susceptibility of gingival tissue to endotoxins from oral bacteria is demonstrated

The finding that certain oral bacteria possess endotoxic properties that may contribute to the pathogenesis of periodontal disease has been demonstrated in studies by investigators in the Laboratory of Microbiology. In previous experiments using endotoxins from oral bacteria, primary toxicity to rabbit skin was demonstrated, and the local Shwartzman reaction of hemorrhagic necrosis was produced by intradermal and intravenous injections of endotoxic preparations. Recognizing the possibility that such endotoxins may have etiologic significance in oral soft tissue diseases, either through primary toxicity or through Shwartzman-like effects, one of the recently isolated endotoxins was tested in rabbit oral mucous membrane. In a study conducted by Drs. A. A. Rizzo and S. E. Mergenhagen, 200 micrograms of a purified endotoxin (lipopolysaccharide) from Veillonella organisms was injected into the gingiva and palatal mucosa of rabbits. Control injections of saline, as well as lipid-carbohydrate-protein products isolated from viridans streptococci, were given at corresponding sites on the opposing sides of the mouth. To provoke the Shwartzman reaction, rabbits were given 125 micrograms of Veillonella endotoxin in the marginal ear vein 12 to 24 hours following local injection. Six hours after intravenous injections animals were sacrificed and processed for histological examination.

Results showed that in rabbits receiving preparatory and provoking injections of endotoxin, gross and histological signs of the classical Shwartzman reaction were evident in the oral mucosa. Control sites given streptococcal products and provoked with intravenous Veillonella endotoxin did not produce this reaction. This demonstration of classic endotoxins in oral bacteria, and the marked susceptibility of gingival tissue to these toxins, offer a better understanding of the inflammation sequence characterizing periodontal disease.

Rice rat shown highly susceptible to periodontal disease

Gross observations of periodontal lesions in the rice rat have revealed the susceptibility of this species to periodontal disease. Grantees reported this year on detailed histologic studies that identify the stages of progression of periodontal disease in these animals.

Dr. Om P. Gupta, University of Illinois, and Dr. James H. Shaw, Harvard University, bred 75 rice rats under controlled conditions, maintaining them on a purified ration for a period ranging from 8 to 30 weeks. The jaws were X-rayed, examined grossly, and then serially sectioned and stained. Subsequent histologic examinations enabled the identification of susceptible and resistant strains. Results showed that 62 percent of the animals were susceptible to periodontal disorders. In addition, the animals in one susceptible litter showed extensive lesions as early as 11 weeks of age, while resistant litters failed to show any appreciable pathology even at 27 weeks. Periodontal lesions were characterized by inflammatory cells and edema in the epithelial and subepithelial layers, dilatation and engorgement of blood vessels, connective tissue edema, peridontal membrane thickening and crestal resorption. About 20 percent of the susceptible animals showed migration, degeneration, and necrosis of gingival and periodontal fibers, and extensive bone resorption.

These studies suggest that the inordinate high susceptibility to periodontal disease in the rice rat is associated with genetic factors, and further establish the unique importance of this animal in periodontal disease research.

CLINICAL INVESTIGATIONS

Oral ulcerated lesions studied in large population groups

Herpes labialis (fever blisters) and aphthous stomatitis (canker sores) are both recurrent painful ulcerations of the mucous tissues of the mouth. A study of these disorders as they occur in a large population group was reported.

The purpose of the investigation, involving some 1,800 persons, was to determine the prevalence of and patient experience with aphthous and herpetic lesions. Participants in the study directed by Dr. I. I Ship included the student bodies of the Schools of Medicine, Dentistry, Dental Hygiene, Veterinary Medicine, Graduate Nursing, and Hospital Nursing of the University of Pennsylvania. Also participating were nursing students at the Philadelphia General Hospital and the Presbyterian Hospital. A specially designed questionaire was employed, and all responses were checked for accuracy by comparison with answers to similar questions on completed medical history forms.

Analysis showed that 38 percent of the students had a history of recurrent herpes labialis with no sex difference noted. On the other hand, a significant sex difference was seen in the 57 percent of females and 52 percent of males that had aphthous ulcerations. In addition these prevalence levels were considerably above those previously reported in population studies by other investigators. Age, racial background, marital status, school, and class differences were not seen in either disease, and students susceptible to episodes of aphthous stomatitis experience more frequent recurrences than those susceptible to herpes labialis. Of particular interest to investigators was the strong relationship noted between emotional factors and aphthous ulcerations. This was seen in both sexes and appeared to be related to the severity of the disease.

NIDR clinical investigator joins survey team in Chile

The Interdepartmental Committee on Nutrition for National Defense conducted a nutrition survey in Chile this year. Dr. Carl J. Witkop, Jr., Chief of the Human Genetics Section, Clinical Investigations Branch, served as dental investigator on the special team composed of 14 American scientists and 14 Chilean health officers.

During the period of study approximately 18 locations were visited, where food samples, dietary histories, and blood and urine samples were collected for analysis. In addition, a total of 1,900 dental and 10,000 medical examinations were made.

Data collected from dental-medical examinations will complement those recently obtained from similar epidemiological studies in other foreign countries where ethnic, geographic, and climatic conditions as well as dietary habits vary widely and are in marked contrast with those seen in this country. Significant among the findings in southern and central Chile was the relatively high incidence of both caries and periodontal disease, the latter being associated with the prevalence of heavy calculus deposits. In contrast, it was noted from examinations made in north-central Chile, including the city of La Serna, that caries and periodontal disease were notably less prevalent, the former being associated with a high incidence of dental fluorosis confined to that area.

In observations of oral congenital anomalies it was found that nonfluoride white opacities of the teeth occurred less frequently in the Chilean population than in comparable U.S. population groups. In addition, torus mandibularus, a bony outgrowth on the inside of the mandible, seen in about 15 percent of U.S. populations, was found in only one individual in those examined in Chile. Torus palatanius, a bony overgrowth of the hard palate, common in this country, was rarely seen in Chile.

Geneticist describes hereditary disease

Dr. Carl J. Witkop, Jr., recently described a rare hereditary disease of the oral and ocular tissues before members of pathology and bacteriology groups meeting this year in Memphis, Tenn.

Speaking before a joint meeting of the International Academy of Pathology and the American Association of Pathologists and Bacteriologists, Dr. Witkop reported that the genetic syndrome occurred principally among a collection of family groups in North Carolina and that it appeared to be similar to, and perhaps identical with, the white sponge nevus described by Dr. A. B. Cannon in 1935.

The Cannon type normally involves the vaginal and anal mucosa; however, these sites were not affected in the group surveyed by Dr. Witkop with Dr. John B. Graham and Mr. Clemm R. Shankle of the Department of Pathology, University of North Carolina Medical School, and other investigators from the

Ophthalmology Branch of the National Institute of Neurological Diseases and Blindness.

Termed as "Hereditary Intra-epithelial Dyskeratosis," the disease was characterized by lesions on the buccal mucosa, floor of the mouth, side of the tongue, as well as the bulbar conjunctivae. History, physical findings, histological appearance, and histochemical reactions supported the belief that both oral and ocular symptoms were local manifestations of the same disease process. There were some indications that the syndrome was subject to seasonal exacerbations. Careful examination, however, failed to reveal any evidence that it was due to a local geographic factor such as an allergen or occupational hazard. Other data also tended to eliminate viruses, vitamin deficiencies, and microbial infections as the responsible factors.

NIDR grantees report wound healing acceleration by dilantin sodium

Hyperplasia of the oral gingiva is a common reaction among epileptics following systemic administration of sodium diphenylhydantoinate (dilantin sodium). To explore the theory that the compound might accelerate the healing of gingival and other wounds through enhanced collagenization, a controlled study of the effect of dilantin sodium on the tensile strength of healing wounds was carried out by grantees at the Indiana University School of Dentistry. The study, as reported by Drs. W. G. Shafer, R. E. Beatty, and W. B. Davis, consisted of three groups of 60-day-old male albino rats, each group subdivided equally to serve as experimental and control. Experimental animals in group I received 50 milligrams per day of dilantin sodium by stomach tube. Experimental animals in groups II and III received 25 milligrams per day dissolved in special diluent and injected intramuscularly. Control animals received no drug, and all animals participating in the study were maintained under identical conditions of diet and quarters.

Dilantin sodium was administered for 18 days before induction of experimental wounds in both experimentals and controls. Three to four days postoperatively, the tensile strength of wounds was tested on strips of tissue that had been cut at right angles to the initial incision. With one end of the strip held stationary, bromoform was added to a cup suspended from the other end of the tissue strip, and values were recorded as ml. of bromoform required to cause separation of the wound. Findings in the respective three experimental groups were 147, 127, and 76 percent greater than those in the companion control groups.

Thus, it was demonstrated that the systemic administration of dilantin sodium produces a dramatic increase in tensile strength of healing wounds in rats and appears to be the same basic reaction that accounts for gingival hyperplasia in epileptics receiving this anticonvalescent drug.

Malocclusion among Negro children is studied

The incidence of malocclusion in the North American Caucasian population is well documented; however, comparable data on the Negro population, which now comprises about 12 percent of the total U.S. population, have not been reported. Therefore, a survey of Negro children was undertaken this year by NIDR grantees at Howard University.

Malocclusion of the teeth not only interferes with the normal function of mastication, but also causes facial disharmony and invites dental disease. Thus,to render a more complete national profile of this dental abnormality, a survey of Negro children in the Washington, D.C., area was undertaken by Dr. L. A. Altemus of Howard University College of Dentistry in conjunction with the District of Columbia Health Department.

A total of 3,500 area children were examined from which 3,298 were selected for study. These children ranged from ages 12 to 16, each had acquired permanent teeth, and none had received orthodontic treatment during their lifetime. The test group, selected from four junior and senior high schools, included a cross section of all income groups and represented the great racial mixture of theNorth American Negro. The frequency of occurring malocclusion was determined by the widely recognized Angle Method of classification and by counting the teeth that were out of normal alinement.

Tabulation of data showed the frequency of malocclusion to be high in the Negro child population of this country. Approximately 83 percent had improper occlusion of teeth, while 4 percent had nearly perfect occlusion. Thirteen percent had teeth slightly malpositioned, but not requiring orthodontic treatment. There were approximately six malocclusions per child and no significant difference in incidence between sexes was noted. With the one exception that Caucasian children averaged 10 maloccluded teeth per child, these data compared closely with the frequency of occurring malocclusion in the Caucasian child population reported by other investigators.

BIOCHEMICAL STUDIES

Apparent difference in excretion of calcium and radiocalcium is reported

During the course of studying the excretion of certain minerals in rats, NIDR investigators found evidence of unexpected variability in the renal clearance of labeled and unlabeled calcium. These findings of possible significance to metabolic studies employing radiocalcium as a tracer were reported this year. In experiments by Dr. Robert Likins and Miss Doris Craven, Laboratory of Biochemistry, weanling rats (group I) were injected intraperitoneally with a solution containing Ca^{45} and a trace amount of unlabeled calcium. Urine was collected at the end of 30 minutes and 60 minutes, and analyzed for radiocalcium and total calcium. One hour after injection, blood from each animal was also analyzed for Ca^{45} and Ca^{40}. A comparable group of rats (group II) were denied food for 12 hours and the experiment repeated.

Results showed that in the two groups of animals the percent of the injected dose of labeled calcium excreted in the urine was significantly less in the case of the starved rats. On the other hand, the total amount of calcium excreted remained the same in starved and unstarved animals. While a slower absorption of the injected Ca^{45} might logically account for this diminished excretion by group II rats, additional experiments showed that plasma of similarly starved rats contained as much radiocalcium 30 minutes after injection as did nonstarved controls.

Although the explanation for this discrimination against radiocalcium is not readily apparent, there is no reason to believe that the renal clearance rates of Ca^{45} and Ca^{40} differ intrinsically. A possible explanation may lie in a different partitioning of the injected label among the body calcium pools, such as bones.

Dental scientists study the relationship of calcifying minerals to dental decay

It has been a long standing concept that the susceptibility of the teeth to dental decay is determined to a large extent by certain calcifying mineral constituents of the diet. Recent data obtained from studies by dental investigators offer a better understanding of how these minerals actually influence the chemistry of the teeth and caries susceptibility. In experiments by Dr. F. J. McClure and Mr. H. G. McCann, Laboratory of Biochemistry, the ash content (calcium, phosphorus, carbon dioxide, and magnesium) of the teeth and long bones of white rats was studied following maintenance on dietary regimes widely varied in calcium, phosphorus, and magnesium. Results showed that variations in these dietary minerals appreciably affected the chemical composition of certain of the calcifying tissues, particularly those which were undergoing mineralization during the experimental period. However, no correlation could be established with the dental caries experience of the test animals. Of additional significance was that, contrary to previous studies reported in the literature, there was no evidence that the carbon dioxide-phosphorus ratio in dental tissues was a significant factor in the incidence or severity of dental decay.

In those diets, which were supplemented with calcium and phosphorus compounds, variable cariostatic effects were noted with the calcium supplement, whereas the most significant and consistent reduction in decay was closely identified with a dibasic sodium phosphate additive. It is noteworthy that this anticaries action was not related to changes in the calcium, phosphorus, carbon dioxide, and magnesium content of the enamel or dentin.

Scientist suggests presence of new protein in dental enamel

While previously published analyses of enamel protein have shown wide variability, they have at the same time agreed in reporting the presence of large amounts of glycine, proline, and hydroxyproline. Largely from such data it might be concluded that enamel protein belongs to the collagen class. This concept was challenged by a NIDR chemist reporting this year on studies of the protein matrix of human enamel.

Recognizing the possibility that previous samples may have been contaminated with varying amounts of dentine collagen, Dr. Karl A. Piez, Laboratory of Biochemistry, performed a series of complete amino acid analyses of enamel proteins carefully isolated from unerupted third morals. Through the use of special apparatus designed to give precise analysis, it was found that the protein was nearly all soluble in the decalcifying solution. Moreover, the soluble protein contained no hydroxyproline or hydroxylsine and only moderate amounts of glycine indicating that it was not a collagen. While its composition showed several distinctive characteristics, it was unlike any other known protein. The small insoluble residue was similar in composition to the soluble protein if the presence of about one-third collagen is assumed.

Thus, it is suggested that results from previous amino acid analyses were influenced by contamination with dentine collagen as well as losses of enamel protein owing to its solubility.

FLUORIDATION STUDIES

Clinical studies compare the relation of caries susceptibility to fluorine content of enamel

A considerable body of evidence attests to a reduction in enamel solubility following treatment with fluoride solutions. This is believed to result, in large part, from a conversion of the hydroxyapatite of dental enamel to a more stable fluorapatite. Further important research on the cariostatic mechanism of topically applied fluoride has demonstrated large accumulations of fluoride in the extreme outer surfaces of tooth enamel. NIDR grantees reported on studies comparing the increment of fluoride in enamel and the reduction in dental caries resulting from topical fluoride applications.

The research study, consisting of both clinical trials and laboratory analyses, was undertaken by Drs. I. Sundvall-Hagland, Eastman Dental Clinic, Stockholm, Sweden; F. Brudevold, Eastman Dental Dispensary, Rochester, New York; W. D. Armstrong, University of Minnesota, Minneapolis, Minn.; and D. E. Gardner and F. A. Smith, University of Rochester.

Clinical investigations were conducted in Stockholm, Sweden, a city where the water contains 0.09 to 0.11 parts per million natural fluoride. One-half of the dentitions of 107 children, averaging 2 years 8 months of age, were treated 4 times with a 2 percent sodium fluoride solution. Each topical treatment lasted for 4 minutes and all occurred within a period of 15 days. The untreated teeth and the teeth of a group of 102 comparable children who received no fluoride treatment served as controls. The caries reductions after 1, 2 and 3, years were 19, 14, and 7.5 percent when based on a comparison of treated and untreated teeth in the same mouth; and 34, 23, and 12 percent when teeth of untreated children were used as controls.

Laboratory analysis of the exfoliated teeth showed that topical fluoride applications caused an increase of approximately 50 parts per million in the fluoride concentration of the outer portion of the enamel. There was no detectable decrease of fluoride content in the treated enamel during the 3 to 7 years period following treatment.

Investigators study fluoride tablets as caries control measure

Although the fluoridation of public water supplies has become an accepted dental health procedure, one-third of the U.S. population does not have access to communal water supplies and may never reap the benefits of this discovery. For this group one of the alternate means of adding fluorides to the diet, which has received considerable attention, is the use of fluoride tablets. Dr. Francis A. Arnold, Jr., Director, National Institute of Dental Research, has presented results of a long-term study of caries inhibitory effects of fluoride tablets in children. Conducted with Dr. F. J. McClure, Chief, Laboratory of Biochemistry, and Mr. Carl L. White, NIDR statistician, the study concluded that the one-a-day tablet regimen could have a beneficial effect on the teeth of growing children.

The mean numbers of DMF and DEF teeth of 121 children ingesting a daily fluoride tablet were compared with corresponding data previously reported for children using natural fluoride or fluoride-adjusted drinking water. Cariostatic effects of the two procedures appeared to be of generally comparable levels. The tablets, containing 2.21 milligrams of NaF (1.0 milligram of fluoride) did not appear to cause any cosmetically significant fluorosis.

The mean fluoride content of deciduous teeth of children ingesting these tablets was found to be higher than that of children in a nonfluoride area. It also appeared that the fluoride content of teeth increased proportionately with the length of time the tablets were ingested.

Based on data gained during the test program, the investigators concluded that the tablet method, while effective, is not as practical as water fluoridation. Further, the fact that the fluoride content of the "home" water supply must be also known suggests that as a public health procedure this method could best be used in controlled programs supervised by health authorities.

Long-term studies confirm beneficial effects of water fluoridation

This year the Director of NIDR participated in a special ceremony climaxing a 13-year independent fluoridation study in the city of Evanston, Ill.

The community of Evanston initiated its water fluoridation program in 1947 as a result of the recommendations of Dr. H. Trendley Dean, then Director of NIDR. City officials obtained the services of Dr. J. Roy Blayney and colleagues of the University of Chicago's Zoller Memorial Dental Clinic in designing and conducting a long-term evaluation of the research program and its effects.

The subsequent survey of Evanston's school children during the 13-year period revealed notable reductions in decayed, missing, and filled teeth as compared with those of the neighboring, nonfluoridated community of Oak Park, as well as with Evanston records prior to fluoridation. These extensive studies also included such features as chemical and bacterial analyses of saliva, water at the filtration plant and at other points in the pipeline system, tooth and bone specimens, as well as roentgenological examinations of occlusion and other oral features.

The figures reported after more than a decade of study, were based on statistics furnished by the Illinois State Department of Health, also cooperating in the survey. Results showed that children of such ages as to achieve fluoridation benefits had an average of 2.75 fewer decayed teeth than those not participating. The Evanston study adds further credence to the beneficial effects of fluoridation reported in long-term studies by the Public Health Service in Grand Rapids, Mich.; Newburgh, N.Y., and Brantford, Ontario.

CALCIFICATION

Scientists develop technique for in vivo study of calcification

Basic studies in the broad field of mineralization have suggested that "regulators" of calcification, or differences in the reactivity of hard or soft tissue collagens, may be factors determining which of the collagenous tissues do or do not undergo mineralization. New methods enabling in vivo studies of these factors have now been reported by NIDR scientists.

In collaborative studies by Drs. S. E. Mergenhagen, G. R. Martin, A. A. Rizzo, and D. B. Scott, assisted by Mr. D. N. Wright, strips of tail tendon from mature rats were implanted in the peritoneal cavities of young Sprague-Dawley rats. Samples removed at 100, 120, and 160 days were found to be hard on gross examination. Marked calcification was indicated by the typically altered calcium/hydroxyproline ratio, and by the presence in the collagen fibrils of hydroxyapatite crystals as identified by electron diffraction. Tail tendon dissected from these same animals at the times when calcified tendon implants were removed showed no evidence of mineralization. In another experiment gels of reconstituted rabbit skin collagen were also calcified when implanted (either directly or after encapsulation in dialysis bags) into the peritoneal cavities of white rabbits and rats.

The phenomenon of intraperitoneal mineralization gives rise to challenging possibilities for in vivo experimentation with collagen preparations which may be subjected to various treatments prior to implantation, or implanted in combination with agents thought to influence mineralization. Such living "model systems," operating under relatively well defined and controlled conditions, should provide new information on the still undetermined factors and mechanisms involved in calcification.

Dental scientists measure differential uptake and retention of calcium and strontium during calcification

Possible hazards associated with the ingestion of strontium 90 from fallout have stimulated interest in the biochemical behavior and metabolism of calcium and strontium in calcified tissues. Dental investigators at NIDR and the American Dental Association's Research Division, National Bureau of Standards, reported this year on studies of the comparative fixation of Ca and Sr by synthetic hydroxyapatite.

Strontium when taken into the body is a bone seeker and like calcium becomes incorporated into the bones and teeth. In laboratory experiments devised by Dr. R. C. Likins, Mr. H. G. McCann, and Dr. D. B. Scott, NIDR, and Dr. A. S. Posner, NBS, trace amounts of radioactive calcium and strontium were introduced in equal quantities into solutions of calcium phosphate out of which synthetic hydroxyapatite was crystallized. By carrying the precipitation conditions a number of "tagged" samples were produced with crystal sizes ranging from 20 to 4,000 millimicrons.

Geiger counter measurements of the relative amounts of the two radioisotopes present showed there was a progressive discrimination against strontium deposition as the crystals increased in size. The smaller, more quickly formed crystals had approximately the same ratio of Sr^{89} to Ca^{45} as the original precipitating solution. However, experiments to determine the distribution of the respective radioactive isotopes within the crystal showed a preferential concentration of Sr at the surface. These results on synthetic materials using radiotracers may lead to a clearer understanding of the comparative uptake of calcium and strontium in the calcified tissue of the human body. Bone crystals, which resemble in size the very smallest synthetic calcium phosphate mentioned above, have already been shown to show a small but measurable discrimination against the incorporation of Sr^{89} as opposed to Ca^{45} in a series of experiments on laboratory rats.

Current studies of the differential uptake and retention of Ca and Sr in the mineral portion of the exoskeleton of certain lower animals may provide an even better understanding of the biochemical behavior of these ions.

EXPERIMENTAL PATHOLOGY

Preservation and storage of viable tissues.

The preservation and storage of organs and tissues for future use in replacement procedures have become important adjuncts to therapeutic practice. Grantees at New York University College of Dentistry reported on studies of the effects of freezing agents and freezing rates on viable oral tissues.

The effectiveness of glycerol and ethylene glycol in preserving the viability of tooth germs subjected to various freezing temperatures was studied by Dr. R. Gerstner and other NYU investigators by explanting the tissues, after thawing, to tissue cultures, and observing the extent of cellular outgrowth and the degree of internal differentiation.

Molar and incisor tooth germs removed from 15- to 20-day-old rat fetuses were pretreated with various concentrations of the two preservative agents. The specimens were then mounted and sealed in test tubes which were immersed in three selected freezing solutions as follows: liquid nitrogen (−198° C.) for 3 minutes; isopentane cooled in liquid nitrogen (−120° C.) for 3 minutes; and, dry ice in ethyl alcohol (−78° C.) for 15 minutes. Following removal, the tooth germs were quick thawed in Tyrode solution and cultured in Carrel flasks. Viability results were evaluated by the extent and condition of epithelial outgrowth from the enamel organ compared with that of control, nonpretreated, nonfrozen tooth germs also in culture. Differentiation within explants was examined histologically and development was compared with previously established growth norms.

Results showed that glycerol in a 30-percent solution was the most effective pretreatment agent, and the slowest rate of freezing—that is dry ice alcohol at 78° C.—was the least damaging of the freezing solutions employed. Continuation studies on the relationship of freezing temperature to freezing rate as a critical preservation factor may lead to the development of better techniques for the storage and implantation of teeth as well as other vital tissues of the body.

Relation of central nervous system and oral disease studied

For many years dental scientists have been preoccupied with studies of various local and systemic factors in attempts to discern the agents responsible for different oral conditions. Grantees at Tufts University School of Dental Medicine reported on studies of the nervous system as one of the contributing etiologic factors in diseases of the oral cavity.

The purpose of the investigation carried out by Drs. G. Quintarelli and H. H. Chauncey was to determine the effects on the oral cavity of chronic visceral stimulation of the brain stem. Experiments were performed on 17 dogs, 7 of which received traumatic stimulation by means of a blunt probe. Ten additional animals were stimulated with glass beads placed in the sella turcica thereby producing a mild continuous pressure on the tuber cinereum, infundibulum, and mammillary bodies of the nerve system. Six animals served as controls and were operated on in the same manner as the experimental animals but received no cerebral stimulation.

All animals in the first group died by the 11th postoperative day, showing severe hemorrhage of the gastric and intestinal mucosa and superficial erosion of the intestinal tract. No oral lesions were noted. Animals in the second group showed changes beginning on the fourth postoperative day when swelling and hemorrhaging of the oral mucosa was detected. This condition progressed until aphthous-like lesions were evident on the mucosa of the lips, cheeks, and tongue. In many instances, the entire gingival area become edematous and inflamed, with progression to marginal periodotitis. Also noted was gastric bleeding and focal lesions and ulcers in the duodenum and jejunum. Control animals kept in the same environment showed no changes in either the oral cavity or intestinal tract.

Data from this study have clearly demonstrated that irritation of certain areas of the brain stem may effect basic pathologic changes in the oral cavity as well as the gastrointestinal tract. Thus, these investigations open for consideration the possible role that more subtle neurological disorders may play in the general behavior of oral diseases.

GROWTH AND DEVELOPMENT

New technique used in relating congenital deformities to fetal anoxia.

Fetal anoxia, implicated in the genesis of congenital deformities, has previously been studied in pregnant animals made hypoxic through oxygen deprivation. NIDR investigators reported this year on studies specially designed to induce anoxia directly in the fetuses of rats, thus bypassing possible complications resulting from maternal hypoxia. The effects of temporary anoxia upon fetal mortality, and upon the frequency of congenital abnormalities, including cleft palate, were studies by Miss Lee Feild, Dr. S. J. Kreshover, and Mr. J. E. Leiberman. Initially, the onset of gestation was established in 249 Sprague-Dawley rats between 2 and 3 months of age. At periods of gestation ranging from 9 to 17 days, the animals were anesthetized and both uterine horns were exposed through abdominal incision. The circulation to either the right or left uterine horn was occluded by clamping the vascular supply, and the uterus was then returned to the body cavity. (This technique provided both experimental and control fetuses within the same parent animal). After the scheduled period of circulatory arrest, ranging from 10 to 60 minutes, the clamps were removed. The uterus was again returned to body cavity, and the incision was then sutured. One day before expected term delivery, the young were extracted by cesarean section and examined.

Results showed that developmental anomalies occurred only in fetuses of the 169 rats treated between the 12th and 15th days of gestation. Twenty-six of the 507 viable experimental young in this group were deformed, whereas 2 of the 523 viable control young were deformed. The greatest frequency of deformities (17.6 percent) occurred after a 45-minute vascular occlusion on the 15th day. There were 13 instances of palatal clefts, 8 of which occurred in the progeny subjected to anoxia on the 14th day. In addition, there were 18 experimental young with limb defects or other abnormalities, 5 of which also had cleft palates.

Data on fetus mortality showed that a high incidence of death was also related to circulatory interference, particularly after occlusion on the 13th gestational day, and after the longer periods of circulatory arrest.

Bone development in chick embryos altered by tetracycline

Frequently used in clinical practice as a broad-spectrum antibiotic, tetracycline is a compound of wide interest to dentistry, both as a prophylactic measure in oral surgery and because of its potential as a caries inhibitor. Grantees at the New York University College of Dentistry, have now reported on studies to determine the possible effects of tetracycline on skeletal formation. In studies designed by Dr. Gerrit Bevelander and associates to test the effects of tetracycline on growing bone, the compound was injected, in amounts ranging from 0.1 to 2.5 mg., into the yolk-sac of 8-day-old chick embryos. It was observed that the 0.5 dose was at first distributed uniformly throughout the embryo. Twenty-four hours later, however, it appeared exclusively in the calcified portions of the skeleton and was identified by its characteristic fluorescence in the presence of ultraviolet light. The 2.5 mg. injections resulted in a pronounced retardation in overall growth of the 10-, 12-, 14-, and 16-day-old chicks. Microscopic examination of the femurs of embryos treated with this relatively large dose showed the following abnormal characteristics: a marked bending, a reduction in the number of trabeculae, and the degree of mineralization was less than half that observed in normal bones. Additional studies of this family of antibiotics are contemplated in light of their frequent use in dental practice on children during the growth and development period.

EPIDEMIOLOGY

Epidemiologic study of oral disease in relation to nutrition

Surveys to identify patterns of association between nutrition and oral disease have been completed in Alaska, Ethiopia, Peru, Ecuador, and Vietnam. Results of these studies, conducted in cooperation with the Interdepartmental Committee on Nutrition for National Defense, were published in summary form this year. In general, epidemiological studies of foreign and domestic population groups have failed to establish a consistent association of dental caries with a deficiency of any known nutrients. For example, both high and low levels of caries experience in Alaskan Eskimos were associated with high intake of protein, moderate intake of fat, low consumption of carbohydrate, and low plasma level of vitamin A. On the other hand equally low, as well as lower caries prevalence levels were seen in Ethiopians subsisting on a comparatively low-protein, high-carbohydrate cereal diet, high in thiamine; and in Vietnamese on a highly milled rice diet yielding only marginal amounts of thiamine and riboflavin. Also unexplained were the large proportions of individuals in each of the groups that were totally free of dental decay.

Where caries levels in these populations were generally low by U.S. standards, the prevalence and severity of periodontal disease were correspondingly high. For example, in Ethiopia, Ecuador, and Vietnam, the levels of periodontal disease were much above any so far recorded for the continental United States. Deviations from this pattern of prevalence were noticed among primitive groups of Alaskan Eskimos and the Ecuadorian Indians, where a reduction in periodontal disease was related to higher thiamine excretions and lower levels of plasma vitamin A. Elsewhere in Alaska, and generally in Peru, periodontal disease levels were comparable with those seen in the United States among people of low socioeconomic status.

Epidemiology studies include Seventh Day Adventist children

Previously reported epidemiologic studies of dental disease in Seventh Day Adventist children have indicated a significantly lower evidence of dental caries than noted in other population groups. NIDR investigators have recently completed studies which assessed the caries experience of Adventist and non-Adventist children under more comparable environmental conditions.

In studies conducted by Dr. C. J. Donnelly, Epidemiology and Biometry Branch, a total of 290 Adventist children and 1,438 non-Adventist children, all lifetime residents of Prince Georges and Montgomery Counties in Maryland, were examined for dental caries. The children were 6 through 14 years of age and all had received fluoride adjusted drinking water since 1952. Sex and age distribution in the two groups, as well as general environmental conditions, were quite comparable.

Results, based on examination for decayed, missing, and filled teeth, showed that there was little difference between the 6- to 9-year-old children in the two groups. These age categories benefited most from the 7 years of fluoridation. However, in the 10 through 14 year categories, there was a 40-percent discrepancy in the mean number of DMF teeth in favor of the Adventist children.

Data from this study suggest further investigation of a possible caries inhibitory factor in the Adventist way of life. Recognizing that fluoridation may have rendered imperceptible such an inhibitory factor, particularly in the younger children, it is planned to continue with parallel studies in areas where caries attack is not influenced by the ingestion of waterborne fluoride.

PROGRAM HIGHLIGHTS

Conference of graduate training program directors sponsored by NIDR

A serious shortage of dental teachers and researchers in the decade ahead has now been confirmed in studies by the American Dental Association and special consultants to the Senate Appropriations Committee. To consider this problem, the National Institute of Dental Research called together the directors of established graduate training centers in July 1960, for discussion of program objectives and expanded efforts in the basic sciences and clinical dentistry.

Speaking before program directors and members of the National Advisory Dental Research Council convened at Western Reserve University, Dr. F. A. Arnold, Jr., Director, NIDR, pointed out that in the next 10 years, a minimum of 4,700 new faculty members will be needed in the basic and clinical science departments of our Nation's dental schools, where today only one-fifth of the faculty members teach full time. Research and teaching manpower needs will mount at a rate of 500 trained individuals a year, Dr. Arnold predicted, and all areas of dental activity—particularly teaching and research—will expand at less than an optimum rate if this central problem remains unresolved. As estimated by the Council on Dental Education, ADA, the cost of training manpower commensurate with needs, under the Federal grant and fellowship programs, is expected to total \$12½ million annually based on today's dollar value.

Highlighting the 2-day program were presentations by prominent figures in the fields of dental education and research. Subjects included: curriculums for graduate clinical and basic science training, part-time versus full-time training, recruitment methods and resources, and the influence of graduate training programs on dental education. New concepts in curriculum design and recruitment procedures were discussed in light of the demonstrated preference of college graduates for Federal subsidized Ph. D. training, and recent recommendation of Federal assistance for undergraduate dental training for those students interested in research and teaching careers.

American Dental Association to sponsor genetics symposium at NIH

Hereditary factors have long been associated with dental related problems such as defective calcification, malocclusion, cleft lip and palate, periodontal disease and caries susceptibility. Currently emphasizing the difficulty of clarifying the influence of heredity is the evidence that many types of environmental agents can be shown experimentally to produce anomalies identical to those produced by defective genes. To further the study of hereditary factors involving the entire organism and particularly their role in oral malformations and disease, the Council on Dental Research of the American Dental Association in cooperation with the National Institute of Dental Research announced in June, 1960 that it will conduct a grant-supported symposium at the National Institutes of Health early in 1961. The program titled "Symposium on Genetics Related to Oral Health," will feature prominent geneticists, and dental and medical investigators from this country and abroad. Its purpose will be to exchange information on present and proposed studies in genetics, thus stimulating greater progress in the field; acquaint the dental profession with recent developments in genetics; and more clearly defined the following areas: (*a*) recent developments in medical genetics, (*b*) hereditable diseases of dental interest, and (*c*) genetic methods applicable to the investigation of intrinsic dental disorders.

Research papers presented at the 3-day session will be published in book form to provide dental and medical investigators with comprehensive source material in the expanding field of genetics related to dentistry.

New dental journal is published

The first issue of Dental Progress, a new scientific journal that seeks to bridge the gap between the researcher and the clinician, was published in October 1960. A National Institute of Dental Research grant assisted in the establishment of the new medium designed to complement the existing, more specialized journals in the field of dentistry.

With an almost explosive increase in the number of research grants beginning in 1957 (fivefold increase over 1956), the National Advisory Dental Research Council was not unmindful of the impact this unprecedented support would have in ensuing years on the existing family of professional dental journals. Therefore, in 1957, the Council appointed a Publication Committee to study the broad problem of communication within the profession, with particular emphasis on ways and means to accelerate the prompt reporting of new research data.

In June 1959, the Advisory Council, acting on recommendations of its Publication Committee, and in consideration of the particular need for a new medium of broad interest to complement the more specialized journals, recommended the award of a grant to the University of Chicago Press to assist in the establishment and publication of Dental Progress. This grant was approved by the Surgeon General in July 1959.

WEDNESDAY, MARCH 29, 1961.

ALLERGY AND INFECTIOUS DISEASE ACTIVITIES

WITNESSES

DR. JUSTIN M. ANDREWS, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	3,237	3,767	4,056
Positions other than permanent	28	38	45
Other personnel compensation	98	89	81
Total personnel compensation	3,364	3,894	4,182
12 Personnel benefits	181	218	233
21 Travel and transportation of persons	110	143	165
22 Transportation of things	51	62	75
23 Rent, communications, and utilities	72	82	97
24 Printing and reproduction	4	7	10
25 Other services	838	435	465
Payment to "National Institutes of Health management fund"	2,424	2,858	3,204
26 Supplies and materials	688	745	778
31 Equipment	99	262	322
41 Grants, subsidies, and contributions	25,632	33,740	34,764
Subtotal	33,463	42,446	44,295
Deduct quarters and subsistence charges	10	10	10
Total obligations	33,453	42,436	44,285

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	546	631	667
Full-time equivalent of other positions	5	6	6
Average number of all employees	521	557	606
Number of employees at end of year	559	615	659
Average GS grade	6.1	6.7	6.7
Average GS salary	$5,388	$6,039	$6,047
Average salary of ungraded positions		$4,269	$4,269

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(*a*) Research	20, 992	27, 550	28, 074
(*b*) Fellowships	1, 065	1, 400	1, 400
(*c*) Training	3, 621	4, 790	5, 290
Total, grants	25, 677	33, 740	34, 764
2. Direct operations:			
(*a*) Research	6, 894	8, 427	8, 698
(*b*) Review and approval of grants	393	558	596
(*c*) Administration	188	208	227
Total, direct operations	7, 475	9, 193	9, 521
Total program costs	33, 153	42, 933	44, 285
3. Relation of costs to obligations:			
Costs financed from obligations of other years, net (−)		−498	
Obligations incurred for costs of other years, net	300		
Total obligations	33, 453	42, 435	44, 285
Financing:			
Comparative transfers to other accounts	572	850	
Unobligated balance lapsing	29	714	
New obligational authority (appropriation)	34, 054	44, 000	44, 285

GENERAL STATEMENT

Mr. FOGARTY. The committee will come to order. Do you have a statement for the committee?

Dr. ANDREWS. Yes, sir; I would like to summarize it, if I may, and make a few remarks about our general program, which I think will be of interest to you.

Mr. FOGARTY. All right.

(The statement follows:)

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, PUBLIC HEALTH SERVICE

Mr. Chairman and members of the committee, the purpose of this statement is to summarize and place in perspective the principal developments in the research programs conducted or supported by the National Institute of Allergy and Infectious Diseases.

Few areas in medicine cover so much territory and present so many implications for the full range of biosciences as the disciplines encompassed by microbiology. The knowledge and skills represented here are often referred to as the "underpinnings" for all of medical research. They are as indispensable to understanding the enigma of cancer as they are to shrinking our ignorance of the common cold. The same is true of other health problems. Without the immunologist and the virologist, for example, our most exciting leads in rheumatic and neurologic disease would fail of critical examination and vigorous prosecution.

What is emphasized here is a major and inescapable conclusion: medical research can maintain momentum and productivity only so long as its broadest discipline, microbiology, remains in a healthy state. Without thoughtful and understanding support of this central resource, the effort the Nation is making to improve the health of its citizens will lose some of its most vital meaning.

IMMUNOLOGY

The progress made in the past year by microbiologists fully justifies a spirit of optimism and hope. In no area is this more evident than in microbiology's most basic discipline: immunology. This is aptly symbolized by the award of this year's Nobel Prize in medicine to two scientists—one English and the other

Australian—for their brilliant contributions to the immunology of tissue transplants.

The implications of such work for surgical medicine need no elaboration. Much has been accomplished to date in the use of tissue transplants to achieve restoration of form and function to the human body. But there is much that remains to be learned about the basic mechanisms underlying the rejection or acceptance of tissue transplants—knowledge vitally needed in devising techniques for the improvement of tissue transplantation.

The work of these two researchers—Sir Frank Macfarlane Burnet, of Australia, whose insights supplied the theoretical basis for transplant immunology; and Dr. Peter Brian Medawar, of Britain, whose experimental studies proved the validity of Burnet's theories—has provided opportunities for scientists throughout the world to bring nearer the day when tissue, and even whole-organ transplantation can be successfully carried out.

Dr. Medawar's current studies at the University of London, dealing with the immunochemistry of isoantigens (the cell substances responsible for the acceptance or rejection of tissue) are being supported by a grant from the National Institute of Allergy and Infectious Diseases.

Recent accomplishments in immunology are especially gratifying when we remember that it was only 5 years ago that this Institute embarked on a new program to stimulate interest in and support of research in immunology and the closely related discipline of allergy. At that time, the entire bloc of research grants in allergy-immunology at the National Institutes of Health amounted to nine projects totaling $75,000. Today the comparable figure is $4,500,000, in support of 149 grants in allergy and 131 grants in immunology.

Five years ago a training grants program in this field was nonexistent. Today the Institute supports 35 training grants in allergy-immunology, amounting to $1,200,000. Fellowships have likewise expanded from 3 in 1956 to 42 today, for a total of $250,000.

One of the areas of immunological research which has forged ahead impressively in the past year has been fluorescence microscopy and its application to rapid diagnosis of disease. In connection with malaria, scientists of this Institute recently reported development of a diagnostic test, employing fluorescent antibody techniques, which may enable a single laboratory worker to screen for malaria a vastly increased number of suspects in a single day.

The new test represents the first recorded instance in which malaria parasites have been viewed by this method. As in other tests of this type, antibodies from the blood of a malaria suspect are labeled with a special fluorescent dye and the antibodies then applied to a blood smear containing malaria parasites. The labeled antibodies couple with the parasites, and when the latter are stimulated with ultraviolet light, they glow a bright yellow color.

The scientists report that the picture presented under the fluorescence microscope is such that it may be possible for a photoelectric cell to detect the glowing malaria parasites. Consequently, they are now exploring the possibility of feeding slides of individual test specimens serially through an electronically controlled scanning microscope for the detection of parasites in large-scale surveys.

At the Institute's Rocky Mountain Laboratory the fluorescent antibody technique has found additional use in identifying Colorado tick fever, a virus disease which has assumed greater importance in recent years throughout the Western States, and have also succeeded in applying the same technique to the diagnosis of Rocky Mountain spotted fever.

At the University of Wisconsin, Institute grantees have applied the fluorescent antibody technique to basic virus studies aimed at determining the precise site of intracellular production of antigen. Three viruses (Newcastle, Sendai, and mumps) were observed through an entire cycle of infectivity. Specific viral antigen was visible in the cells as granules distributed throughout the cytoplasm. This was not true of the influenza virus, in which antigen was first seen by fluorescence in the nucleus, followed by later appearance in the cytoplasm.

A simple and rapid diagnostic test for lupus erythematosus, a connective tissue disease related to rheumatoid arthritis, was developed in the past year by an Institute scientist. The test is similar to the bentonite flocculation test originally devised by the same scientist against rheumatoid arthritis and trichinosis. The new test appears to be more specific in diagnosing lupus erythematosus than the widely used L.E. cell test.

INTERNATIONAL RESEARCH CENTERS

Less than 6 months after the 86th Congress had passed the International Health Act of 1960, its intention had already begun to be fulfilled. By November 23, 1960, NIH had approved the applications of four American universities to sponsor international centers for medical research and training. Program developments already initiated by this Institute provided a foundation for this beginning and for future developments.

Since 1958 the Institute's National Advisory Allergy and Infectious Diseases Council and its training grants committee had been developing a program to insure that a few academic institutions, with special competence, would be conducting tropical medicine training programs. These projects would provide for a U.S. university to establish a relationship with a foreign institution to insure extensive supervised field and foreign research experience for the trainees. This program effort culminated in June 1960 with the approval of application from six universities.

This basis was enlarged to encompass the specific purpose of the international medical research and training program to advance international status of the health sciences through cooperative enterprises. The program will provide training on a reciprocal basis, with Americans assigned to foreign institutions and foreign trainees to our institutions.

The four universities approved November 23, 1960, for participation in this international endeavor, Johns Hopkins University, the University of Maryland, the University of California, and Tulane University, had met the requirements of the previous program. The sound plans submitted by the University of California (Berkeley) serve as an example of what can be expected from the participating universities.

The university medical school has already secured "enthusiastic" agreements to cooperate in the training program from the following institutions: NAMRU–2, Taipei, Taiwan; the University of Hong Kong; the University of Malaya, Singapore; the University of Malaya, Kuala Lumpur; Institute for Medical Research, Kuala Lumpur; Queensland Institute of Medical Research, Brisbane; and the University of Melbourne.

The University has set up comprehensive plans to utilize the readiness of its own staff and the cooperation of the Pacific area universities. It has idientfied itself closely with the needs of the United States and the interests of the U.S. Public Health Service in the international centers, stating:

"The current philosophy of the San Francisco campus is directly relevant to the proposed developments. In the belief that education should be oriented more emphatically toward man himself, and that the greatest scientific advances in understanding man have come through studies developing out of medicine, the authorities are actively exploring the development of a college of letters and science in association with the medical center in San Francisco, with the essential study of man as a common goal. * * *"

VIRUS DISEASES

In terms of incidence, viruses are responsible for more human diseases than any other known cause. Illnesses for which they are responsible range from the ubiquitous upper respiratory infections, generally self-limiting but vastly expensive in public health and economic terms, to the encephalitides, an example of which is the epidemic of eastern equine encephalitis that struck New Jersey in 1959 with a high death rate.

In addition to the direct causal relationship of viruses to known infectious diseases, increasingly they are being studied to assess the extent to which they may be involved in cancer, neurological disorders, and heart disease.

One of the widely heralded advances in virology in the past year is the first experimental vaccine of demonstrated effectiveness against measles. Investigators supported in part by this Institute reported with others on an effective vaccine for this disease, which in recent years has been responsible for more deaths in children than poliomyelitis. Although measles is usually a mild disease, some cases develop serious complications, including pneumonia, impairment of hearing and sight, and brain damage. With an attack rate of 70 to 95 percent among persons susceptible to the disease, and with a birth rate in the United States of 4 million annually, the number liable to severe complications is considerable.

Trials to date of the new vaccine, still in the experimental stage, have demonstrated its effectiveness in the prevention of measles. The investigators are extending laboratory and clinical studies in order to refine further the minimal side effects of the present vaccine, which include fever and loss of appetite. Improvement of this new vaccine is expected to result in a product of comparable potency but reduced side effects which can safely be offered to the large segment of our population that needs it. If no setbacks are encountered in field trials recently undertaken abroad, the vaccine will probably be submitted for Federal licensing in the near future.

The acute respiratory infections represent another area in which a vaccine or vaccines are much needed. This group of illnesses is of such complexity, however, that much field and laboratory work must be accomplished before vaccination against any substantial portion of these infections will become feasible. Relationships between the many respiratory viruses, already identified, and their clinical symptoms must be defined in specific terms, i.e., susceptible groups, frequency of attack, duration of immunity, and populations involved.

Work of this kind is in progress and serves to underscore the complicated nature of the problem. As of last year, the causative agent of approximately 35 percent of these illnesses had been described by scientists of this Institute in studies carried on over a period of several years with nursery-age children. With the additional analysis of the respiratory syncytial and primary atypical pneumonia viruses in recent months, a substantial percentage—in the neighborhood of 10 to 15 percent—can now be added to this figure.

A similar project on respiratory illness is presently underway at the NIH Clinical Center. Laboratory and clinical scientists are collaborating in a study of volunteer prison inmates, housed at the clinical center, who are being inoculated with respiratory viruses. While it is too early to comment on the significance of preliminary findings, we believe that there are obvious advantages to studying this problem in a controlled atmosphere, with highly trained personnel in constant supervision and with modern laboratory equipment immediately available. Hopefully, we anticipate a harvest of detailed, exact information from this research that would not be obtainable from other studies less comprehensive or less well controlled.

One of the specific viral agents in which there has been much recent interest is the Eaton virus, originally described in 1944. The role played by this virus in human respiratory disease and its relation to primary atypical pneumonia has been of interest to microbiologists for several years.

Recently Institute scientists demonstrated the importance of this agent as a cause of severe lower respiratory tract illness in both youngsters and adults. In one investigation 10 percent of all infants and children hospitalized with pneumonia were found infected with the Eaton virus. In another study, Eaton virus was incriminated in 51 percent of all pneumonia cases at a Marine recruit training center during a 1-year period.

We hope that the controversy regarding the effects of antibiotic treatment on primary atypical pneumonia involving the Eaton virus will prove to be resolved as a result of a cooperative study between the U.S. Navy and this Institute. An article describing the findings of this study has been submitted to a scientific journal for publication.

One of the encephalitides under study in this Institute, western equine encephalitis (WEE), may attack either man or horses and is closely related to the mosquito-borne encephalitis causing the epidemic with high fatality that occurred in New Jersey in 1959. The most extensive recorded human epidemic of western equine encephalitis occurred in 1941. It affected over 3,000 persons in 2 Western States and adjacent Canadian Provinces, with a mortality rate of 8 to 15 percent.

A major unsolved problem in the ecology of this arthropod-borne disease is the method by which the virus maintains itself during the winter. Within recent months, scientists at our Rocky Mountain Laboratory have uncovered evidence which may aid in clarifying this question. Under test conditions resembling those in nature, they were able to show that the garter snake may harbor the encephalitis virus during the winter months. To provide more conclusive evidence for the role of snakes in the maintenance of the disease, an effort will now be made to isolate the virus from reptiles actually collected in the field.

In the study of viruses as they may relate to cancer, the ability of the mouse polyoma virus to produce multiple tumors in mice and other rodents is of intense interest and has stimulated extensive studies in many laboratories. Research by scientists of this Institute on the behavior of polyoma virus in the mouse has been carried out in three different field environments: in densely populated tenement areas of a large city, on farms producing grain and livestock, and in grain mills located in rural communities. Each presents a different ecology, but in each one focal environmental contamination appears to be quite important to survival and persistence of polyoma infection. Although serologic studies do not support the hypothesis that polyoma virus can infect man, widespread access of humans to the polyoma agent through mouse-contaminated environments makes consideration of possible human infection of more than academic interest.

Comprehensive serological studies of over 75 common viruses became feasible in the past year as the result of successful commercial production of experimental lots of antigens achieved under the direction of Institute scientists. These antigens are needed in the collaborative study sponsored by the National Institute of Neurological Diseases and Blindness, which is conducting a unique long-range investigation of the newborn and their mothers. From this should come new understanding of normal and abnormal birth processes. Before definitive seroepidemiologic surveys of virus infections in relation to birth defects can be monitored, antigens and test procedures must be evaluated to achieve quantitative information on sensitivity and specificity. With the availability of these new antigens, a good beginning on this aspect of the study has been made.

PARASITIC DISEASES

Parasitic diseases, whether considered individually or as a collective entity, remain a major obstacle to human progress in vast areas of the world. Programs to reduce these diseases have gained the interest and financial support of the U.S. Government and have made encouraging progress. A little more than a decade ago, malaria, for example, struck 300 million people annually and killed 3 million. These figures have since been cut in half as a result of vigorous control programs. It has been apparent since as early as 1951, however, that mosquito carriers of malaria could develop resistance to insecticides used in the programs. This factor and other inadequacies of malaria controls point to the need for more effective preventive and treatment drugs to supplement use of insecticides.

Institute scientists stress that new drugs are required and that old ones must be better used. Their concern is heightened by evidence that resistance is developing against drugs currently in wide use. A recent instance was the discovery in South America of a malaria strain which is resistant to chloroquine, a drug of choice in the suppression and clinical treatment of the disease.

Other reevaluations of the disease are indicated. A recent laboratory feat by scientists of this Institute directly challenges the concept of malaria investigators throughout the world that types of malaria which infect animals cannot be transmitted to man by the bite of an infected mosquito. After demonstrating that such transmission is possible, our scientists expressed the belief that "research on lower monkey malarias, with particular regard to the possible existence of reservoirs of human infection, or sources of reinfection of man with new strains, is necessary as an essential adjunct to the present malaria eradication program." They also projected a detailed study of monkey malarias and a reexamination of the entire question of host specificity in this disease.

A direct followup to this laboratory discovery was the establishment of a field research project in Malaya by three NIAID staff members in cooperation with that country's Institute for Medical Research and the U.S. Army medical research unit at Kuala Lumpur.

A number of intensive studies were initiated during the year by Institute scientists to improve or test the effect of various antimalarials. Included were studies of drug combinations, the influence of nutritional deficiencies on antimalarial activity, and the influence of cortisone on antimalarial activity.

Mention should be made of the development of a new diagnostic test for malaria which is described in greater detail in another section of this statement. The test, which our scientists emphasize is of a preliminary nature, may make it possible for a single laboratory worker to screen many more suspects for malaria in a single day than was heretofore possible.

Approximately 150 million people in Africa, Asia, the Caribbean area, and South America suffer from schistosomiasis. It is caused by several species of small worms called blood flukes. The disease is easily acquired by penetration of the parasite into the skin of bathers or others entering fresh water in the endemic areas. The results can be severely crippling to the individual, and in underdeveloped countries where incidence is high the capacity for economic growth is thereby limited.

The cost of eradicating schistosomiasis is not economically feasiable for most of these countries because of the comparatively large quantity of chemical needed for destruction of the snail vector of the disease. However, a series of laboratory experiments by Institute scientists indicate that very low concentrations of sodium pentachlorophenate will drastically diminish the fecundity of the snail and lower the viability of the eggs that are produced.

The treatment of the disease also has been unsatisfactory in spite of the many years spent in searching for better drugs. If the results of recent Institute experimental work with infected animals can be transferred to the human form of schistosomiasis, improved therapy for its victims may be anticipated. In laboratory tests the efficacy of stibophen, a drug commonly used in the treatment of this disease, was greatly improved when infected mice were fed an enriched, purified semisynthetic diet. In one trial the average worm reduction in mice on the diet was 95 percent, compared with 12 percent in mice on a regular commercial laboratory diet.

Filariasis is a mosquito-transmitted parasitic disease that afflicts an estimated quarter of a billion persons in tropical areas. Within recent years sporadic cases have been reported in the Southern United States. It is caused by slender threadworms which parasitize the lymphatic tissues in man. The minute larvae of these worms circulate in the bloodstream, from which they are easily transferred to others by the mosquito or are discharged into standing water and again reach man after a stage of existence in tiny water organisms. Unfortunately, the breeding habits of certain of these mosquito species enable them to evade the lethal effects of DDT.

A recent discovery by Institute scientists offers new diagnostic and therapeutic possibilities in the campaign against the disease. Their test findings, based in part on their previous experiments, showed that it is possible by a simple fluorescent method to trace the movements of the filarial worm in patients receiving dosages of the antibiotic, tetracycline.

They were able to proceed with their experiments from the knowledge that tetracycline fluoresces a yellow-gold color when exposed to ultraviolet light and that tetracycline is absorbed by the filarial organism. In addition to tracing the movements of the worms under the skin of a patient in the Bethesda Clinical Center, their tests suggested more effective antifilarial uses for tetracycline.

STAPHYLOCOCCAL INFECTIONS

Although it is impossible at the present time to present a comprehensive set of statistics for staphylococcal infections, the magnitude of the problem in the United States is now well recognized. These infections are widespread in the obstetrical divisions of many hospitals and cause havoc in the operating room. In the medical service wards they constitute a severe hazard to patients afflicted with other serious diseases. In the latter instance, the debilitated status of these patients, together with the relative inability of the antibiotics to control resistant staphyloccal strains, contributes to an excessively high mortality. Equally grave, many infected patients fail to develop overt evidence of disease until after discharge from the hospital. These infections are then disseminated into the community at large.

As a result of the special action taken by Congress in providing an additional $1 million in 1959 for research into the problem of antibiotic-resistant staphyloccal infections, this Institute was able to step up impressively the volume of research activity in this area. These investigations have now begun to yield the data necessary to permit a more effect attack on the staphylococcal problem.

Recently, one of our grant-supported scientists at the New York Hospital-Cornell Medical Center completed a series of investigations of great potential importance in clarifying our understanding of how staphylococcal epidemics develop in hospital nurseries. Briefly, his study revealed that any newborn infant infected with staphylococci may fall into one of two distinct groups, one comparatively harmless, the other, highly contagious. Infants in this latter group are literally surrounded by bacteria. So marked is this phenomenon that the term "cloud babies" has been coined to describe it. According to the investigators, this latter group of infants, although small in number, plays an extremely significant role in the explosive outbreaks of staphylococcal disease occasionally occurring in the nursery or in the community.

Interestingly enough, these infants present no overt signs of disease themselves. The investigator found that a factor only partly understood—one which is independent of the staphylococcus itself and which has a distinct epidemiology of its own—is responsible for the "cloud" phenomenon. This factor appears to consist of the presence, along with the staphylococci, of a number of respiratory viruses occasionally encountered in the newborn.

The exact nature of this association is not yet determined and will require further investigation. It is possible that the effect of the viruses on the respiratory tissues is to facilitate a huge increase in numbers of bacteria, i.e., staphylococci. Under these conditions, the air passages may be modified as to quantity of secretion or quality, affording the possibility of a vastly increased dispersion of the bacteria—thus the explosive outbreaks. Whatever the final explanation, this important new epidemiological lead has already brought fresh insights into an area which has for a long time remained obscure and discouraging to epidemiologists.

For the Nation's practicing physicians, the most important development of the past year in this area has been the clinical testing of a new synthetic penicillin which is apparently effective against many forms of staphylococcus shown to be resistant to a variety of antibiotics. The new penicillin, designated "Staphcillin" by Bristol Laboratories of Syracuse, N.Y., is the product of some highly original joint research by scientists of Britain's Beecham Group, Ltd., and Bristol Laboratories. Participation by this Institute was limited to clinical testing and biochemical characterization of the drug. Results have been dramatic. In the clinical trials our scientists administered the drug to 10 patients with a variety of staphylococcal and streptococcal infections. These were chronic and severe cases which had been treated over long periods of time with other antibiotics, without success. Each of these apparently hopeless patients responded to Staphcillin in a spectacular fashion. The result of this trial, and similar results obtained by other investigators participating in the cooperative study, indicate that the drug is now ready for general use in clinical medicine. Its ultimate value will not be known until it has been employed for extensive periods in the treatment of staphylococcal infections.

At the University of Utah one of our grantees has announced a new diagnostic test for determining the pathogenicity of various staphylococcal species isolated from clinical sources His procedure grew out of an observation that pathogenic strains of this organism may be differentiated from harmless strains by their selective ability to react with the chemical salt, tellurite The older tube coagulase test had achieved wide acceptance as the single most accurate laboratory indicator of potential pathogenicity of the staphylococcus. The new test, however, is said to be fully as accurate and is, in addition, a simpler method, more convenient to carry out, and extremely economical.

CYSTIC FIBROSIS

The second phase of a three-part study designed to assess the magnitude of the cystic fibrosis problem in the United States has been completed by the Children's Bureau in cooperation with the National Office of Vital Statistics. The primary purpose of this pilot survey in three New England States was to develop and test procedures to be used in a future national survey. Massachusetts, New Hampshire, and Vermont were chosen to test the techniques devised for the survey because the area contains a large urban, rural, and semirural population and a relatively well defined medical care area centered in a big city, Boston.

The pilot survey, which is financed by a research contract from the National Institute of Allergy and Infectious Diseases, is considered primarily of importance as a testing ground for the sampling techniques for evaluating the problem on a nationwide scale. Secondarily, it has produced some statistics of real interest. For example, data on the 671 patients reported in the three-State sample indicate that cystic fibrosis can no longer be regarded as a regularly fatal illness of early childhood, as was believed originally when the disease was described and given its name some 20 years ago. Almost 50 percent of the 169 deaths occurring in the study population in the period from 1952 through 1959 were patients aged 5 years and over. Almost 18 percent of the deaths were in patients 10 years and older. Only 24 percent of the fatalities occurred in infants.

Another significant statistic which has emerged from the pilot study concerns incidence of the disease. Estimates have ranged widely, from a high of 1 in 600 live births to a low of 1 in 3,700. Based on the current study, the total incidence of cystic fibrosis among residents in the pilot area is estimated to be at least 1 in 2,300 live births.

Although the number of cases on which the study is based is frequently too small to yield reliable conclusions, the value of the present analysis lies as much in the presentation of methods used for studying data on the magnitude of the cystic fibrosis problem as it does on the presentation of significant information per se. When the survey is extended to cover the entire Nation, as is planned for the coming year, the pretested methods of data collection and evaluation of the present survey should prove invaluable.

MIDDLE AMERICA RESEARCH UNIT

The Middle America Research Unit, cosponsored in the Panama Canal Zone by the Public Health Service and the Walter Reed Army Institute of Research, is conducting its unique studies in two major areas, mycology and arthropod-borne virus diseases.

The research program of the Mycology Section has markedly increased awareness in the Canal Zone of the fungal disease, histoplasmosis, a lung infection frequently mistaken for tuberculosis and which occurs in the United States as well as Latin America. Within a period of 18 months, three disseminated cases have been recognized, two fatal and one treated successfully. Prior to this time, only one fatal case had been described since the original report of cases which appeared more than 50 years ago. Ecological and epidemiological studies of the soil of Panama have produced 16 isolates of *H. capsulatum*, the causative organism of the disease, which grows as a mold in soil. Before the establishment of the Mycology Section in Panama only a single positive soil sample was recorded. Further confirmation of the wide dissemination of this fungus in nature has come from its repeated recovery from the organs of trapped ground mammals.

Histoplasmin skin testing continues to be a major tool for measuring the prevalence of the infection in Panama. More than 9,000 children 6 to 19 years of age have been surveyed by this method. As expected, the percentage of reactors increases progressively with age, ranging from 13 to 58 percent among 6-year olds and from 68 to 92 percent in the oldest group, depending on where they live. Among preschool children, 6 months to 6 years of age, there was a definite increase in hypersensitivity, beginning with the 3-year olds.

During the first year of a projected 3-year study on the ecology of ARBOR (arthropod-borne) viruses in a tropical rain forest, cooperative research with the Gorgas Memorial Laboratory, major emphasis has been on virus isolation in suckling mice and hamster kidney cell cultures. Fourteen virus strains have been isolated at MARU from 412 pools and 63,000 specimens provided by Gorgas.

The prevalence of antibodies to Eastern equine encephalitis virus in horses and man has now been determined, allowing an evaluation of the relative utility of several serological methods applicable to this kind of study. In 460 humans tested, the incidence of EEE antibodies—indicating past exposure to the disease—increased with advancing age (0.8 percent under 10 years, with progressive increase to 9 percent in the 41–50 year group).

Previously an outbreak of a fatal disease of swine caused by encephalomyocarditis virus was described by MARU scientists, the outstanding lesion of which was acute myocarditis. Following epidemiological observations that suggested contaminated food as a source of infection, experiments were undertaken to reproduce the disease in young pigs by feeding them virus. Following infection, pigs developed high antibody levels during convalescence and myocardial fibrosis was found at autopsy.

Human sera from the Panamanian population was also tested for this virus. A substantial proportion has demonstrated EMC virus infection, with antibodies more common in younger age groups.

A new entomological approach to the problem of the maintenance and transmission of animal viruses is now under way at MARU. This is the first serious attempt to explore the possible role of chiggers and other related arthropods of the American tropics in spreading disease to man. Knowledge gained from this 2-year project hopefully may supply some much-needed answers concerning how viruses are spread and continue to exist in nature.

THE GORGAS MEMORIAL LABORATORY

Scientists of the Gorgas Memorial Laboratory in the Republic of Panama are continuing their studies of the diseases problems of special importance to Middle America and of potential significance to our own and neighboring countries. Since its establishment over 30 years ago, this medical research unit of the Gorgas Memorial Institute of Tropical and Preventive Medicine has been concerned with such endemic diseases as yellow fever and malaria, and in recent years has contributed significant information on viruses in the tropics. Last year, the Congress acknowledged the value of the work of the Laboratory by increasing its annual allocation for operation and maintenance from $150,000 to $250,000 and providing $500,000 for construction of new facilities.

The Gorgas Memorial Laboratory is exploiting its unique opportunity to study the ecology of arthropod-borne viruses in three separate field projects, each with definite and distinct objectives. One of these is a virological exploration of a well-defined tropical rain forest climate, ranging from the collection of mosquitoes and sandflies, the bleeding of wild and domestic mammals, birds, and reptiles, the surveying of the blood parasites of birds, to studying patients with febrile illness of unknown origin in whom a search is being made for a possible viral cause of their diseases. This multifaceted research is being supported by an NIH grant, and is a cooperative effort of Gorgas and of the Middle America Research Unit of this Institute.

In Cerro Azul, an area where sylvan yellow fever was found in 1948 and again in 1956, the Gorgas Memorial Laboratory has established a mosquito-collecting station in the hope of detecting any future waves of sylvan yellow fever which would menace the Canal Zone and Central America.

There has been little change in the malaria pattern in Panama over the past year. The demonstration, however, of continued transmission of the disease in spite of a residual spraying program points up the importance of the kind of long-term active malaria research typified by Gorgas Memorial Laboratory studies.

Research on the leishmaniasis transmission-reservoir problem in Panama, under investigation for many years, continued during 1960. In clinical studies of the disease, preliminary results of the use of pyrimethamine therapy show considerable promise, particularly in children in whom with this treatment there is prompt and complete healing of lesions. In the laboratory, scientists of a newly established U.S. Naval Medical Science Unit have successfully grown in tissue culture, for the first time, the causative organism of American leishmaniasis, *Leishmania brasiliensis*. The new unit is studying tropical disease problems of particular concern to the U.S. Navy, including Chagas' disease and others caused by blood parasites of man.

Dr. Walter A. Bloedorn, president of the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc., has submitted a copy of the operating budget for the Gorgas Memorial Laboratory. As spokesman for ths Institute before Congress, I am requesting that the maximum funds authorized by Congress be made available to the Institute during 1962.

SUPPORT OF INSTITUTE PROGRAMS

The 1962 amended request for the National Institute of Allergy and Infectious Diseases is a total of $48,322,000. This compares with $54 million[1] for 1961. The allowance for 1962 will enable the Institute to maintain all activities at their present level with over half of the requested increases in the research grants activity; and the balance of the increase spread between training grants, direct research, review and approval of grants, and administration. The request for 1962 is distributed among program activities as follows:

Grants:	
Research	$31, 637, 000
Fellowships	1, 400, 000
Training	5, 290, 000
Subtotal, grants	38, 327, 000
Direct operations:	
Research	8, 978, 000
Review and approval of grants	773, 000
Administration	244, 000
Subtotal, direct operations	9, 995, 000
Total 1962 amended request	48, 322, 000

[1] Less comparative transfer of $850,000.

Dr. ANDREWS. Mr. Chairman and members of the committee, few areas in medicine cover so much territory and present so many implications for the full range of biosciences as the disciplines encompassed by microbiology, the longtime basic interest of this Institute.

VIRUS DISEASES

In terms of incidence, viruses are responsible for more human disease than any other known cause. A wide range of virus problems are under study by our Institute scientists and grantees. One widely heralded advance this year is the first experimental vaccine of demonstrated effectiveness against measles. Part of the extensive research which led to that accomplishment was supported by a grant from this Institute.

You may be interested in knowing, parenthetically, that our Council at its last meeting approved a grant to investigators at the University of Maryland to appriase the effectiveness of this vaccine on a large sample of Baltimore schoolchildren this school year.

In support of the International Health Act of 1960, we have approved the applications of four American universities to sponsor international centers for medical research and research training. Programs previously initiated by this Institute provided a foundation for this auspicious beginning.

PARASITIC DISEASES

Parasitic diseases continue to represent a major obstacle to human progress in vast areas of the world in spite of vigorous programs to improve the situation. A recent laboratory feat by our scientists directly challenges the concept that some malarias of animals cannot be transmitted to man by the bite of infected mosquitoes. Research on this new aspect of the problem is underway here and abroad.

As spokesman before Congress for the Gorgas Memorial Laboratory, Republic of Panama, I request that the maximum funds authorized be made available to that Laboratory. These amount to $250,000.

1962 BUDGET

The 1962 amended request for the National Institute of Allergy and Infectious Diseases is a total of $48,322,000. This compares with $43,150,000 for 1961. The allowance for 1962 will enable the Institute to maintain all activities at their present levels with over half of the requested increases in the research grants activity; and the balance of the increase spread between training grants, direct research, review and approval of grants, and administration.

INCIDENCE OF INFECTIOUS DISEASES AND ALLERGIES

I should like to start out as far as programs are concerned by calling your attention to very recent appraisals of the importance of infectious diseases and allergy disorders in this country. According to the findings just released by the U.S. National Health Survey, two-thirds of the acute illnesses and one-fifth of the chronic diseases were considered to be caused by infection or allergy. From the same source, the total cost of infectious, parasitic, and allergic disability was computed to be about $2½ billion for fiscal 1958. These data are included in a tabular summary which has been submitted to this subcommittee.

Also, in the February issue of Public Health Reports, our National Office of Vital Statistics presents data showing significant increases during recent years in the numbers of reported deaths and of death rates in this country from septicemia, infections of the newborn, and from such specified causes of infection as those involving skin, lungs, kidneys, and the central nervous system.

CYSTIC FIBROSIS

Next I should like to bring you up to date with respect to our recent findings concerning cystic fibrosis, which I know is of interest to you. You will recall that this is a heritable disease, primarily of white children, involving altered metabolism of the pancreas, liver, and exocrine glands in general, and that death from it is almost always caused by an overwhelming pulmonary infection with staphylococcal organisms. It is with prevention of this terminal event that our Institute is primarily concerned. Our sister Institute of Arthritis and Metabolic Diseases supports and carries on research concerning the other noninfectious aspects of this disease.

Our research grants in this area amount to about $294,000. One of them, by way of example, made to a group of clinical investigators at Harvard, is concerned with the feasibility of diagnosing this disease in newborn infants. When babies are born with intestinal obstruction, emergency surgery is usually necessary. Cystic fibrosis is one of the causes of intestinal blockage. It would be helpful to know before operating if the patient did have cystic fibrosis, as this would dictate a type of anesthesia which would not irritate or dry out the delicate lung tissues in which postoperative staphylococcal infection is so likely to occur with fatal results in cystic patients.

DIAGNOSIS

Using an appropriate modification of the sweat test devised by Dr. Paul d'St. Agnesi in the Arthritis Institute, the grantees found that it was possible to diagnose cystic fibrosis as early as 1 day after birth. The real difficulty in this was getting enough perspiration from these day-old infants; but by a combination of chemical and electrical stimulation, it turned out to be possible. This procedure has already been lifesaving with reference to the postoperative complications that I have mentioned.

Mr. FOGARTY. Is this test carried on in every hospital in the country?

Dr. ANDREWS. I do not know if it is carried on in every hospital in the country, but I am sure it must have very general use.

Mr. FOGARTY. Do you think it should be?

Dr. ANDREWS. Yes, I think it should be. As a matter of fact, relative to this, I can say that the work which we have been doing with the Children's Bureau to obtain some idea of the prevalence of cystic fibrosis has had the effect of interesting investigators and has aroused and extended physician interest in this disease wherever it has been studied. This is indicated, I think, by the increased publications concerning this disease, and in our own case by more case referrals to the Clinical Center.

Mr. FOGARTY. By the way, how are you getting along with the Children's Bureau?

Dr. ANDREWS. Fine. The information which it has supplied for the end of the second year gives us a partial answer, at least, to the question which you asked. The Bureau has found that this disease occurs in the population about once per 2,300 births. Other estimates have ranged from a low of 1 per 3,700 to a high of 1 per 600 live births. Those in the lower ranges have been based upon studies designed with more care to avoid sampling and observational bias, and I suppose these are more truly indicative of the actual situation. Accordingly, we may say, as an interim response to your question, that cystic fibrosis has been found to occur generally in 1 out of from 2,300 to 3,700 live births, which would mean that the incidence is about 4 times that of the birth of triplets and from 2 to 3 times the occurrence of paralytic polio in youngsters of comparable age.

I should point out, however, that even at the lowest ratio of incidence mentioned, cystic fibrosis is presently identified as the most frequent lethal genetic disease among white children.

Mr. FOGARTY. Why do you say "white children"?

Dr. ANDREWS. Because it does not occur in colored children. There has been no record I can find about it. Certainly, if it occurs, it is with extreme rarity. I doubt whether it occurs at all.

Our clinical investigators in this Institute see some 20 to 30 patients with cystic fibrosis each year and thus have opportunities to follow the course of this disease in response to various treatments. Some of these children have been in and out of our hospital unit repeatedly for 4 years or more. Until this last year, it had proved well-nigh impossible, due to the development of drug resistance, to eradicate staphylococci from the pulmonary tract. This year the use of a new synthetic penicillin developed jointly by British and American investigators (Beecham Group, Ltd., Great Britain, and the Bristol Laboratories in Syracuse, N.Y.) has produced more encouraging results. This product, known as Staphcillin, a trade name, in this country, was shown in our Institute and by other investigators to be remarkably resistant to penicillinase, the enzyme produced by resistant staphylococci and which destroys natural penicillin. Using a combination of inhaled, aerosolized synthetic penicillin and intramuscular injections of the same drug, it has been possible to reduce pulmonary staphylococcal populations in those children to zero, at least for brief periods. This is regarded as the most promising development thus far in the therapy of cystic fibrosis.

A special report on cystic fibrosis is being submitted to this subcommittee.

(The report referred to follows:)

CYSTIC FIBROSIS

Research on cystic fibrosis at the National Institutes of Health is the joint responsibility of two Institutes, both of which are conducting studies in their own laboratories while they also support investigators elsewhere under research grant programs. The National Institute of Arthritis and Metabolic Diseases is concerned primarily with basic investigations dealing with the underlying defect presented by the disease, i.e., the dysfunction of the exocrine glands. At the National Institute of Allergy and Infectious Diseases, cystic fibrosis studies emphasize the therapeutic problems associated with the disease and particularly the critical problem of controlling the pulmonary infections which chronically threaten patients.

This hereditary disease of children and adolescents has been recognized as a separate disorder only since 1938, when a Columbia University pathologist, Dr.

Dorothy Anderson, gave the first complete description of cystic fibrosis based on 49 cases assembled from the literature and from autopsy records at New York's Babies Hospital (Columbia University Medical Center).

The fundamental defect responsible for the failure of the exocrine glands to function normally is unknown. (The exocrine system is comprised of two groups: the non-mucus-producing glands which involve sweat, tears, and salivary secretions and the mucus-producing glands which are associated with the pancreas, small intestine, lungs, and liver.)

In fully manifested cases of cystic fibrosis the typical findings are chronic lung disease, pancreatic deficiencies, abnormally high sodium and chloride content of sweat, and occasionally cirrhosis of the liver. However, there are wide variations in the clinical picture of the disease, depending upon the degree of involvement of the various organs or glandular systems.

Two years ago the National Institutes of Health brought together leading investigators from this country and abroad to explore current knowledge in this field and to assess the research status of cystic fibrosis. The proceedings of this International Research Conference on Cystic Fibrosis, comprising scientific presentations and discussions by experts in the field, were published in the past year and distributed to all interested scientists. This volume is a much-welcomed reference source which summarizes the accumulated knowledge of the last 20 years and poses many provocative questions for investigators now at work on the highly complex problems posed by this disease.

ACTIVITIES OF THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

The principal aim of the cystic fibrosis (CF) research carried on by the National Institute of Arthritis and Metabolic Diseases is to uncover the basic biochemical defect responsible for the abnormal functioning of the exocrine glands. Much of this research deals with fundamental problems, such as, How does the body normally synthesize mucus secretions? and How do the abnormal secretions of CF patients differ, both chemically and physically, from normal secretions? Are the abnormal changes present in mucus secretions throughout the body or only in certain secretions? What causes the salt content of sweat, tears, and saliva to be elevated?

In the Institute's new Pediatric Metabolism Branch, studies which may answer some of these basic questions are underway. Under the direction of Dr. Paul di Sant'Agnese, one of the leading experts in cystic fibrosis research, scientists are studying the biochemical pathways by which mucoproteins are synthesized, and are analyzing the components of secretions taken from CF patients. Special emphasis is being placed on any factors which may affect the solubility of the mucus secretions, and their physical characteristics. Improved types of treatment are also under intensive study and new drugs that appear beneficial receive careful evaluation in cystic fibrosis patients.

Since cystic fibrosis is an inherited disease, Institute researchers are also interested in the genetic basis of the disorder and how "homozygous" patients differ from "heterozygous" ones. Homozygous patients are those who have inherited a full disease potential from both parents whereas heterozygous ones have inherited a partial disease endowment, presumably from one parent only.

Institute research with relatives of cystic fibrosis patients has shown that 20 to 30 percent of the relatives have abnormally high salt levels in their perspiration, and thus exhibit a partial manifestation of the disease. Likewise, some adults who suffer from chronic pulmonary infections have high salt levels and may in reality be heterozygous CF patients. Since their hereditary endowment for cystic fibrosis was only partial, these individuals do not develop all the manifestations of the disease to their fullest extent and therefore manage to reach adult age.

NIAMD quantitative studies of the high salt level in the sweat of cystic fibrosis patients are being carried out under different conditions of stress in order to correlate the amount of inherited disease potential with the degree of abnormality found in the patients. These studies have shown that homozygous patients cannot reduce their high sweat salt levels even under conditions of extreme salt deprivation and when supported with steroid hormone therapy. On the other hand, the heterozygous patients are able to conserve salt under these conditions (this is consistent with the observation that they survive better in hot weather). In cystic fibrosis prolonged heat exposure may lead to possibly fatal "heat exhaustion" in non-salt-sparing patients.

In addition to the various projects underway at Bethesda, 30 research project grants have been authorized this year for studies on cystic fibrosis at research centers elsewhere. They range in subject from the microchemistry of the sweat glands to investigations of the eye changes that are now being seen in certain cystic fibrosis patients.

These eye changes are a relatively recent finding and what relationship they have to the disease is not yet clear. Institute grantees at the Babies Hospital of the Presbyterian Hospital, New York, first became aware of complaints referable to impaired vision and abnormal ocular findings several years ago, and since then all cystic fibrosis patients admitted to the hospital have had careful ophthalmological investigation. These examinations revealed such abnormalities as engorgement of the retinal veins, retinal hemorrhages and swelling of the optic nerve. In come children the changes were associated with impaired vision, while in others they could be detected only by detailed opthalmological examination. Preliminary studies indicated only two constant factors: (1) the presence of moderate to severe pulmonary disease, and (2) increased levels of gamma globulin in cerebrospinal fluid and blood serum.

Studies of these eye changes are also being performed by Institute scientists, in collaboration with the National Institute of Neurological Diseases and Blindness. There are several possible explanations for the eye changes, such as chronic hypoxia or oxygen deficiency, a bleeding tendency, or some disturbance of serum globulin, but no constant abnormality has yet been found.

In other grant-supported research, attempts are being made to improve the effectiveness of presently used forms of treatment. A new approach to treatment, loosening the sticky mucus in the lungs by applying vibration to the chest wall, has been reported by physicians at the University of Pennsylvania School of Medicine. Although the method is still in the experimental stage, it may be of considerable value in bringing about increased drainage and augmenting the present use of antibiotic-containing aerosols to combat lung infections.

ACTIVITIES OF THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DSIEASES

Congenital intestinal obstruction in the newborn, resulting from a thickening in the secretion of the intestinal glands, represents a surgical emergency in which preoperative diagnosis of the cause of the obstruction is important. This condition, known as meconium ileus, is found in 10 to 15 percent of all newborn infants with cystic fibrosis.

Successful application of the sweat test, originally developed by Dr. Paul A. di Sant'Agnese, now with the National Institute of Arthritis and Metabolic Diseases, to the diagnosis of intestinal obstruction in the newborn, was reported by a group of Harvard investigators, whose work is supported by a grant from the National Institute of Allergy and Infectious Diseases. The sweat test, which measures the sodium and chloride levels in the sweat of suspect children has been a major diagnostic criterion for cystic fibrosis for several years. Abnormal elevation of these levels is one of the reliable indications of the disease. The test was performed on a group of 37 babies in the first 4 days of life among whom were several with intestinal obstruction. This was done in an effort to arrive at a positive diagnosis of suspected cystic fibrosis (with abnormal meconium obstruction and associated changes) before attempted surgical exploration.

On the basis of this study the authors reported that the defect in the sweat glands of cystic fibrosis can be detected as early as one day of age. Case reports were presented concerning the six babies with intestinal obstruction to whom the sweat test was applied shortly after admission to the hospital. Abnormal elevations of sodium and chloride levels were detected in four of these, who later showed other manifestations of cystic fibrosis. The others with normal perspiration had other intestinal abnormalities but not fibrocystic disease. Thirty-one babies of the same age served as a control group.

The authors point out that it is helpful for the surgeon to know before operating for intestinal obstruction whether or not he is likely to encounter true meconium ileus. When the basic condition is cystic fibrosis, he may select a type of anesthesia avoiding undue irritation or drying of the bronchial mucosa. This is important because the most frequent cause of deterioration of the patient after successful surgical correction of meconium ileus is the early development of respiratory complication.

In another investigation completed in the past year, the U.S. Children's Bureau, working in cooperation with the National Office of Vital Statistics, compiled new data on the incidence of cystic fibrosis. This is the second phase of a three-part study designed to assess the magnitude of the cystic fibrosis problem in the United States. The study is being financed by the National Institute of Allergy and Infectious Diseases under a special contract.

The pilot survey was conducted in three New England States and its main purpose was to develop and test procedures which will form the basis for a future national survey. The States serving as the test areas—Massachusetts, New Hampshire, and Vermont—were chosen because they offer a large urban, rural, and semirural population as well as a relatively well defined medical care area in a metropolitan center, Boston.

While the main purpose was to test the sampling techniques for nationwide use later, the study has yielded statistics of some interest. Data collected on 671 patients in the 3-State sample confirm the general belief of investigators that cystic fibrosis can no longer be considered an invariably fatal disease of early infancy and childhood. Almost 50 percent of the 169 deaths in the study population during the 1952–59 period were patients aged 5 years and over. About 18 percent of the fatalities involved patients 10 years and older. Only 24 percent of the deaths occurred in infants.

Data also emerged from the pilot study concerning the incidence of cystic fibrosis, estimates of which in the past have ranged from a low of 1 in 3,700 live births to a high of 1 in 600. Based on the 3-state sample, the incidence of the disease in the study population was estimated to be 1 in 2,300 live births.

The most significant development of the past year in studies conducted in the Bethesda Laboratories of the National Institute of Allergy and Infectious Diseases was the successful clinical trial of a new synthetic penicillin jointly developed by scientists of Beecham Group Ltd., Great Britain, and the Bristol Laboratories, Syracuse, N.Y. The new drug, named Staphcillin by the American firm, proved strikingly effective against staphylococcal infections which had failed to respond to treatment with conventional antibiotics.

This development has direct implications for cystic fibrosis inasmuch as the most common and troublesome pathogen involved in the recurrent pulmonary infections of CF patients is the staphylococcus. Approximately 90 percent of the deaths from cystic fibrosis are due to pulmonary infections, a fact which underlines the critical importance of improving clinical management of this aspect of the disease.

The results obtained by our scientists with this new antistaphylococcal drug were presented at a symposium sponsored by the State University of New York, Syracuse, N.Y., in the past year. Detailed findings are included in a special report on staphylococcal infections prepared February 1961 by the National Institute of Allergy and Infectious Diseases as background information in connection with the fiscal year 1962 appropriations hearings.

STAPHYLOCOCCAL DISEASES

Turning now to the staphylococcal diseases in general, I should like to refer again to the new preparation, dimethoxyphenyl penicillin, or "Staphcillin," which we have used for the treatment of staphylococcal complications of cystic fibrosis. This has also been employed in our own clinical facilities in the treatment of a wide variety of staphylococcal diseases including septicemia, endocarditis, arthritis, pneumonia, and abscesses. All patients treated have lived thus far and have shown improvement or cure, with only an occasional relapse, and without the development of drug resistance over a period of several months. The only untoward effects thus far have been occasional skin rashes and other evidences of allergic reaction which occur also with the previous penicillin treatments.

A special report on staphylococcal infections is being submitted to your subcommittee.

Mr. Fogarty. Will you give us some of the highlights of that report?

Dr. Andrews. I would be glad to.

Mr. Fogarty. I asked earlier in the hearings about a 31-year-old woman who just had a baby and who got one of these infections and died in 2 or 3 days.

I always thought it was confined pretty much to children.

Dr. Andrews. This occurs at almost any age, in fact at all ages. It is perhaps more critical in individuals with low resistance, and this means it occurs most frequently in very young children. Very aged people also have a high prevalence of staphylococcal infections.

Mr. Fogarty. I thought a couple years ago you had this problem licked.

Dr. Andrews. It had not been licked, and I do not know that this new drug is the final answer.

Mr. Fogarty. Tell us some of the things you are doing and things which should be done.

Dr. Andrews. We have been working particularly with children in our hospital unit. Many of these youngsters come back—I am not speaking of cystic fibrosis now but of staphylococcal disease—over long periods of time. We had one little fellow named Danny. Danny was 3 years old when he first came to the clinical center. His abscesses were lanced and drained repeatedly. He had peritonitis. He had pneumonia. He had all kinds of boils and abscesses, and the poor little fellow was in bad shape most of the time. Many of our young doctors were quite unhappy about the fact that Danny showed up again and again and they had to open his boils and drain his abscesses repeatedly.

They gave him this new preparation, Staphcillin, and toward the end of the year, Danny was able to go home from the hospital in time for Christmas and he is now in school for the first time in his life. This accomplishment is representative of the successful staphylococcal treatments which are now happening. We think these achievements are very thrilling.

MALARIA IN MONKEYS

A new area of research which developed this year in our Institute concerns the infectibility to man of certain types of malaria in monkeys. This was discovered, curiously enough, by the accidental infection of our own employees in our Memphis laboratories. Shortly thereafter the very same thing occurred in the laboratories of two other investigators where the same strains of simian malaria were being used. It is remarkable indeed that this is not known to have occurred before, because one strain was isolated in 1935 and the other in 1957. These have been maintained in monkeys by blood or mosquito transfer ever since.

These observations have led to numerous and elaborate experiments with Federal prisoner volunteers. They have established without doubt the fact that certain species of malaria parasites from lower animals can survive and multiply in and be transmitted to man, and from man to monkeys, by mosquitoes under experimental conditions which simulate those in nature. Recent observations suggest that both strains are becoming more adaptable to human hosts than they were in the earlier transfers.

The two strains of parasites used in these observations both originated in Malayan monkeys. This has led to the establishment of a field station in Malaya to study strains and species of malaria parasites from both monkeys and man, hoping to determine more adequately their interinfectibility and other characteristics.

Somewhat comparable observations have been made recently with the natural malarias of chimpanzees and man in Liberia by some of our research grantees who have demonstrated some limited cross-infectivity. Other investigators have interested themselves in this problem in the past, but the apparent difficulty of previous researchers in producing cross-infection led malariologists to presume that such phenomena were of little or no significance in nature. This, indeed, may still be the correct appraisal of the situation. It is too early, in my opinion, to make any sweeping conclusions concerning this possibility, and the practical implications of the current observations with reference, for example, to worldwide malaria eradication, but it is obvious that definitive and adequate research in this area is urgently required.

A special report on simian malaria is being submitted to this subcommittee.

MALARIA RESEARCH WITH PRISONER VOLUNTEERS

I should like to say a few words about prisoner volunteers because they have become increasingly important in our work this past year.

The use of prisoner volunteers for malaria research is not new, but until recently this has been carried on within Federal or other prisons. Its success has suggested the use of these individuals for other experimental purposes, in the course of which it was found desirable and feasible to transfer prisoner volunteers, with their guards, to our clinical center for types of more sophisticated clinical observations that could not be made in penitentiaries. By this means, for example, it has been possible to carry on adequately controlled experiments with reference to agents suspected of causing acute respiratory diseases. A virtually standardized technique has been developed utilizing the special manpower and the instrumental facilities of the clinical center, which justifies the expectation that more advanced research with reference to the common cold and other respiratory infections and allergic processes may be possible in the future.

More than 100 inmate volunteers, as these individuals like to be called, at the Atlanta Penitentiary were used during the year in studying the infectibility of simian malaria parasites to man. About 70 others have participated in controlled studies on respiratory disease agents at the clinical center.

ALLERGY AND IMMUNOLOGY

The application of chemical and physical methods to the analysis of house dust has resulted in a clearer definition of the components of this disreputable conglomerate which are responsible for allergic reactions in sensitive individuals. The active constituents extracted appear to be a heterogeneous mixture of acidic polysaccharides. This demonstration is a long step toward preparation of materials to alleviate the discomfort of patients suffering from house dust allergies. These extractive techniques may be applied also to other substances which cause allergies in the hope that the offending component can be specifically identified and protected against.

Using the technique of fluorescent antibody staining, serum from recovered patients has been shown to react with human malaria parasites. This technique holds some prospect of developing a more rapid, sensitive, and simplified procedure for diagnosing malaria and perhaps even for identifying the various strains of parasites found in man and in lower animals.

The uncommon but important condition of allergic thyroiditis has been reproduced in experimental guinea pigs by injection of thyroid extract. This condition is clearly shown to be an autoimmune disease, that is, due to antibodies produced against tissue of the animal's own body. It has become increasingly clear that this type of reaction may explain the cause of a number of diseases of which the etiology was formerly unknown.

This last week a new clinical allergy project was commenced and patients admitted to the Clinical Center with a condition known as hereditary, angioneurotic edema (chronic urticaria) or "giant hives." This study attempts to determine the role in the development of this disease, of a newly described serum enzyme which increases the permeability of capillaries. This investigation, being made in collaboration with scientists of the National Heart Institute, may help to explain this puzzling disease and, hopefully, lead to other investigations of allergic urticaria.

Until this year, program activities in immunology have been almost exclusively basic; that is, they have not dealt with the clinical aspects of allergy and immunology. During 1960, it was possible to activate a Clinical Immunology Section with an experienced clinician in charge, who will work in conjunction with our Laboratory of Clinical Investigation. It is expected that studies may be pursued involving the immunologic aspects of such diseases as lupus erythematosus, nephritis, chronic thyroiditis, and others in which an autoimmune basis is suspected.

VIROLOGY AND RESPIRATORY DISEASES

I should like to say a few words about virology and respiratory diseases. Medical investigators at the Harvard School of Public Health have just completed the gargantuan research task of following the health and disease experience of 67 local boys and the same number of girls from birth until their 18th birthday. They observed and reported many facts of interest over this long period of observation—but the one to which I want to call attention at present is that 83 percent of the total illnesses of this group of 134 persons during 18 years were respiratory.

The range of disease which may affect the respiratory tissues is fantastically great, and runs the gamut from congested, snuffy noses to the lethal pneumonias and tuberculosis. Intensive research on the genesis of the "common cold" was being carried on when I was a graduate student 35 years ago—and still is today—though the techniques of investigation have advanced greatly.

Mr. FOGARTY. Have you made any headway?

Dr. ANDREWS. I think so. For one thing, it has been increasingly possible to identify various components of the common cold complex. This is a highly multiple causation which results in approximately similar diseases.

Mr. FOGARTY. When you found that out, what did you do about it?

Dr. ANDREWS. Everyone hopes that after they get an exhaustive list of the causes of these diseases it will be possible to make vaccines which can be used to prevent them. I must say, however, that the multiple vaccines we have used thus far in the Children's Hospital and a local orphanage have not been conspicuously successful.

One of the difficulties is that the more causative agents in these vaccines, the greater the likelihood of interference of one with the others. With the exception of the influenza component, which has been included in our common-cold vaccine, we have not seen any very hopeful results. However, the influenza vaccine did prevent influenzal sickness in the vaccinated children.

We have two new respiratory disease agents which will illustrate just what I am talking about. One of these is known to virologists as the respiratory syncytial virus. It produces bronchiolitis, that is, inflammation of the terminal air-sacs of the lungs; in many instances it leads to pneumonia. This virus is estimated to be the cause of some 20 percent of all lower respiratory illnesses in children. It was discovered during cooperative studies of our own scientists with local pediatricians at the Children's Hospital in Washington, D.C., and at Junior Village, a nearby orphanage.

I should like, at this point, to pay tribute to our local welfare agencies and hospital staffs who so willingly provide opportunities for our NIAID medical scientists to explore with them some of the afflictions which present themselves on a mass basis in these establishments. These cooperative studies with local pediatricians in children's institutions have been major factors in pushing forward the frontiers of our knowledge of the common respiratory infections. It is now possible to identify the viral causes of some 60 percent of all respiratory illnesses suffered by babies and little children in hospitals. This places us closer to the point where it should be possible to reduce the gap in our knowledge of viral etiology and to proceed further with the development of vaccines for the prevention of these distressing illnesses.

Our virologists, with the Navy medical staff at the Parris Island Marine Base, have investigated cases of primary atypical pneumonia and have demonstrated conclusively that the so-called "Eaton agent" is the cause of widespread infection among recruits. This disease agent was isolated from sputum and lung tissue in 1944, and since then has been suspected to be the cause of disease in recruits in military camps and the general population. It is only recently, through the newly developed techniques of immunofluorescence and tissue culture, that it has been conclusively shown to be the actual cause of disease. Epidemiologists and virologists from our Institute and from the Navy have studied cooperatively this form of pneumonia which at certain critical times has been so important in the training camps of our Armed Forces.

An interesting point is that the agent may be widespread in the camps and cause only minor but significant illness in the majority of those it infects; but in approximately 1 in 30 infected individuals, it produces a very severe pneumonia. Fortunately this agent—which is not in the category of the ordinary viruses—is susceptible to antibiotic therapy, and a new tetracycline compound, dimethylchlortetracycline, is effective in the treatment of the soldiers and sailors who suffer with this illness.

CANCER VIRUSES

I should like to say just a word about the cancer viruses. Increasing interest in viruses as a cause of cancer has stimulated the development of new and improved laboratory tools for working with these viruses, and the study of the natural history of tumor viruses in animal populations. One of these agents, the polyoma virus, has been found by our virologists to be widely disseminated in mouse colonies in many different places, from New York City to remote farms and feed mills. Furthermore it has become increasingly clear that advances in the knowledge of the role of viruses in cancer will be retarded until the problem of latent viral infection of experimental animals, particularly mice, is solved.

New research methods have demonstrated that there are at least six viruses commonly found naturally infecting experimental mice. This emphasizes the fact that the methods and techniques which have been used to study viruses as causes of infectious diseases will have to be applied as well to the determination of their role in the production of cancers and tumors. Studies of these conditions in animals should certainly advance the time when causative factors of cancer in humans can be more effectively investigated.

I want to make it abundantly clear that the interest of our Institute in all of these tumor virus agents is in their basic biologic and chemical attributes as viruses, their pathogenic properties, their distribution to nature, and the methods by which they can be identified. Their significance as causes of human cancer will be determined under the suspices of the National Cancer Institute.

OFFSITE INSTALLATIONS

We have four offsite installations, the Rocky Mountain Laboratory in Montana, the Middle America Research Unit in Panama, the Malaria Laboratory in Columbia, S.C., and a fourth in Memphis, Tenn., where cytologic studies of simian malaria parasites and their life cycles have been in progress. The last is being transferred to Chamblee, Ga., near Atlanta to premises recently vacated by the Communicable Disease Center.

Mr. Fogarty. Are you transferring one of these units to that firetrap in Georgia?

Dr. Andrews. I presume these structures are still inflammable but they have reconstructed certain of the buildings. At least one of them is a metal building.

Mr. Fogarty. Off the record.

(Discussion held off the record.)

MEASLES VACCINATION

Mr. Denton. I want to ask you about this vaccination against measles. Just how far along are you with that?

Dr. Andrews. We have tried it on an experimental basis successfully. I am not aware of any large scale trial. This is what will be undertaken shortly by our grantees as mentioned earlier.

Mr. Denton. When you say "experimental," what do you mean by that?

Dr. ANDREWS. I mean that it has been tried on perhaps three or four dozen people here, and a similar number someplace else. When it is to be conclusively tested, it ought to be on a large number, perhaps five or ten thousand children.

Mr. DENTON. Has it been successful?

Dr. ANDREWS. It has been on these small experimental trials. It has produced some unpleasant reactions which have been mitigated to some degree when gamma globulin has to be given along with the vaccine.

Mr. DENTON. Has there been a reaction?

DR. ANDREWS. Yes, there have been some reactions to the vaccine that have been troublesome.

Mr. DENTON. There used to be a vaccine they gave you when you had measles.

Dr. ANDREWS. I believe that was really a convalescent serum containing antibodies which mitigated the severity of the disease to some degree.

Mr. DENTON. I know measles can be very serious.

Dr. ANDREWS. Yes, sir.

Mr. DENTON. You say most cases are mild?

Dr. ANDREWS. This is correct, but over twice as many children die each year from measles complications as from poliomyelitis.

Mr. DENTON. It is the aftereffects?

Dr. ANDREWS. Yes, sir, it is the complications which kill.

Mr. DENTON. I asked somebody this question last year about cancer. They said the virus was inside the cell and antibodies do not do any good. The thing you must do is to get the virus as it goes from cell to cell. Is not the virus inside the cell in measles?

Dr. ANDREWS. Not all the cells of the body. It is selective for various tissues.

Mr. DENTON. How does this serum work? Does it create antibodies?

Dr. ANDREWS. No, sir; it contains antibodies which neutralize the virus; in essence, it kills the virus.

Mr. FOGARTY. You may proceed.

OFFSITE INSTALLATIONS

Dr. ANDREWS. As I indicated previously, we have four offsite installations, the Rocky Mountain Laboratory in Montana, the Middle American Research Unit in Panama, the Malaria Laboratory in Columbia, S.C., and a fourth in Memphis, Tenn., where cytologic studies of simian malaria parasites and their life cycles have been in progress. The last is being transferred to Chamblee, Ga., near Atlanta, to premises recently vacated by the Communicable Disease Center. This will bring together in one municipal area the malaria inoculation research at the Atlanta Penitentiary; the related mosquito-rearing, maintenance, and dissection facilities; and the monkey colony, all of which are necessary in the simian malaria investigations which we regard as being of great importance.

All of these offsite facilities serve to provide space, an essential which is still in short supply at NIH.

ROCKY MOUNTAIN LABORATORY

Research at the Rocky Mountain Laboratory has been directed traditionally toward field studies of arthropod and lower animal borne diseases, endemic in the Western and Northwestern States. In connection with these and other infectious processes, certain basic laboratory explorations have been made.

These last have been concerned with the purification, the chemistry, and the surface properties of viruses, including poliomyelitis virus; the relations of hypersensitivity and humoral immunity, and the role of structural elements—peripheral versus interior cytoplasm—of a wide variety of microorganisms in the immunologic and sensitizing activities of these agents.

The observation, previously reported, that the cell walls of a variety of microbial organisms contain more immunizing properties than do the cell contents has been confirmed in principle in an increasing number of agents. Experimental vaccines prepared from cell-wall extracts have protected laboratory animals against challenge with tularemia and brucellosis.

Field studies in Montana and neighboring States have related to Q fever, tularemia, Colorado tick fever, and other arthropod-borne viral diseases such as western encephalitis.

Colorado tick fever continues to be a vexing and frequently serious problem in certain of the Western and Northwestern States; different lots of ticks collected during the year in Estes Park, Colo., varied in incidence of infection up to 21 percent, thus accounting for the large number of Colorado tick fever cases reported in Colorado each year. An effective vaccine has been prepared from the brains of infected suckling mice and has been shown to be effective in mice. This has been used also in man, and has proved to be both safe and protective, though repeated doses are necessary for prolonged effectiveness.

As reported last year, western equine encephalitis virus can be maintained in garter snakes. It has now been found that this virus will overwinter in these reptiles and that mosquitoes fed upon them in the subsequent spring become virus infected, suggesting that garter snakes or some similar creatures may constitute offseason reservoirs of infection. Thus far, however, no naturally infected snakes have been found.

COLUMBIA, S.C., MALARIA LABORATORY

This laboratory has been identified for many years with the study of malaria chemotherapy, using patients at the South Carolina State Hospital. Its contributions have served as important sources of tested and reliable information on which the Armed Forces and international health agencies have based schedules for the treatment, suppression, and prevention of malaria.

Also it has been the principal source of malaria-parasite-containing materials, used for many years by physicians to inoculate patients who have certain mental disorders to produce controllable fevers believed to be beneficial in the treatment of these diseases. Since the introduction of penicillin, which is useful in treating the same disease chemotherapeutically, fever therapy has been less popular, but it is still considered the treatment of choice by some medical practitioners. Since January 1960, this laboratory has supplied such infectious materials in response to 17 requests.

During the last year, the malaria laboratory has demonstrated that chloroquine, the present antimalarial drug of choice, and certain of its relatives, is no longer effective against a strain of malignant malaria imported from Colombia, South America. This confirms and extends clinical observations made in Texas to the effect that his strain does not respond to the usual doses of this medication.

Additional evidence of the lack of effectiveness of this drug is appearing in other parts of the world. Since some 80 million persons are taking antimalarial treatment in various countries and situations where insecticides cannot be used effectively, this phenomenon could be most serious, especially if it develops that many strains of malaria parasites become resistant to chloroquine and related antimalarial drugs.

MIDDLE AMERICA RESEARCH UNIT

The Middle America Research Unit is now a well-equipped, well-staffed commodious laboratory, established with permanent status in the Panama Canal Zone primarily to study tropical arthropod-borne viral diseases, and certain fungal disorders. The latter activity is sponsored and supported by the Walter Reed Army Institute for Research.

In collaboration with the Gorgas Memorial Laboratory, which is carrying on a grant-supported, 3-year, ecologic study of arthropod-borne viruses in a tropical rain forest, our MARU virologists have identified vesicular stomatitis virus in sand flies of the genus *Phlebotomus*. This virus causes an important disease of cattle and horses in the United States and has been shown on occasion to infect man. MARU scientists also found antibodies against this virus in the blood of persons living in the area where the sandflies occur. Whether or not these individuals experience illnesses of any significance associated with this evidence of infection has not been ascertained.

The most vexatious problem faced by our employees at the MARU is the unavailability of acceptable living accommodations. Commissioned officers may occupy military quarters if available. Civilian scientists are not eligible for these but are obliged to rent expensive and frequently substandard apartments or houses in Panama City. Thus it is increasingly difficult to recruit and retain civilian employees, especially with large families, for duty in the Panama area.

A special report on the Middle America Research Unit is being submitted to this subcommittee.

GORGAS MEMORIAL LABORATORY

I recently had the opportunity of visiting both the Middle America Research Unit and the Gorgas Memorial Laboratory, and it is pleasant to report that each of them has more research activity underway than can be maintained conveniently, and that they find numerous opportunities for cooperation, in both directions.

The previously mentioned Almirante project, conducted with the cooperation of MARU, has involved the collection of huge numbers of insects, jungle mammals, birds, and reptiles from which 25 viral agents have been isolated thus far.

Similar large-scale collections of blood have been made from animals, birds, and reptiles with the object of identifying viruses by means of serology and virus isolation. From the blood of two different species of birds, the little blue heron and a keel-billed toucan, viral isolates were made, recovering Ilheus virus from both. These are the first isolates of this agent from birds, though antibodies related to it were found in the blood of five others.

The other grant-supported project at GML concerns the investigation of sylvatic yellow fever in an area where the virus of this disease was active in 1948 and 1956. Nearly 9,000 mosquitoes were collected during the year and were examined virologically. Four agents were obtained from them but none of these proved to be yellow fever. Three remain unidentified; the fourth was the virus of St. Louis encephalitis.

Thousands of mosquitoes were captured in an area where Eastern encephalomyelitis in horses had occurred. This virus causes sleeping sickness or "brain fever" in man as well as equines. These insects were processed virologically and two agents were isolated which have not been identified, though they did not prove to be the virus of Eastern equine encephalomyelitis.

Other collections of blood were taken from 195 residents in Darien. Antibodies were found against St. Louis encephalitis, Ilheus virus, and yellow fever. In the case of the latter, it is not known whether the antibodies present were the result of natural infection or immunization.

Taxonomic work on mosquitoes has been continued and mosquito colonies of representative forms have been maintained at the Gorgas Laboratory. Many insect vectors—Triatomidae—of Chagas' disease were examined for the presence of trypanosomes; these were found in three species of insects.

Studies on the transmission of cutaneous leishmaniasis were continued in areas where the disease had been endemic. Suckling white mice were found unsuitable for maintaining strains of Leishmania organisms, but hamsters inoculated on the face just above the nose became infected and produced an abundance of organisms.

Sandflies (*Phlebotomus*) were reared successfully in the laboratory for at least 14 generations; this is an unprecedented achievement. They have been infected with Leishmania organisms by the pipette technique of artificial feeding. Feeding on infected rats has given negative results.

Work on the taxonomy of sandflies has continued and 12 new species have been described, mostly from Panama.

The time-honored methods of treating leishmanial ulcers with intramuscular antimony compounds have not been entirely satisfactory. In an effort to develop an oral chemotherapy, pyrimethamine has been tried and shows some promise, especially in children, where the young skin lesions heal promptly and completely. The addition of sulphadimethoxane, principally for its antibacterial action, has been useful in cases where ulcers are grossly infected with bacterial contaminants.

A U.S. Naval Medical Science Unit was reestablished at the Gorgas Memorial Laboratory in September 1959. Such a group existed at the Laboratory from 1939 to 1959. Personnel assigned consist of a Medical Service Corps scientist and a chief hospitalman concerned with parasitologic research. They have been studying the tissue phases of *Trypanosoma cruzi* and of *Leishmania donovani* and *L. bra-*

siliensis. Efforts have been made to grow these agents within tissue cultures, some of which have shown indications of success.

The routine malaria field studies of the Gorgas Laboratory were conducted for their 30th year. The original object of this research was to determine whether malaria could be controlled by drugs alone. Since 1946, a combination of medication for parasitized individuals and residual spraying of all homes by the Republic of Panama Malaria Eradication Service has been employed. In spite of these activities, malaria appears to maintain itself at about the same level in the Chagres River villages, year after year.

You will be interested in knowing something about the timetable for the new building at the Gorgas Memorial Laboratory. I was told by its director, Dr. Carl M. Johnson, that he expects to have plans completed by June, the contracts let by September, ground broken by October 1961, and the building probably completed by October 1962.

I accompanied Dr. Johnson, his technician, and a Panama dermatologist on a field trip to an area where cutaneous leishmaniasis, or "Oriental sore," was highly prevalent. Some 40 to 50 infected individuals came for diagnosis and treatment. All lesions were flash-photographed, and scrapings were made from new cases in efforts to establish etiologic diagnosis.

By means of diagnosing and treating infected persons in different localities, Dr. Johnson has ascertained those areas in which this disfiguring skin lesion is highly prevalent. Efforts are then made to collect Phlebotomus sand flies from animals, such as burros, which serve as attractants to the flies. Surprisingly high percentages of sand flies have been found infected with leishmanial flagellates in nature; I believe this is the first time that this phenomenon has been observed, though obviously it must have been going on for a long time. Some of the fly collectors have been bitten by these insects and have developed oriental sores.

These events constitute abundant evidence that Phlebotomus is the vector of cutaneous leishmaniasis in Central America as it is elsewhere. This has been generally assumed but had never been proven.

The Annual Report of the Gorgas Memorial Laboratory was distributed recently, and I expect has been received by this subcommittee. If not, I will be glad to see that copies are supplied.

I should like to add one other point with reference to our interest in Panama and Central America, which is, speaking in behalf of Dr. Carl M. Johnson, Director of the Gorgas Memorial Laboratory in Panama, and Dr. Alexis Shelakov, Director of the Middle America Research Unit in the Canal Zone, that they would be most heartily delighted to have you, or anyone of your representatives, pay a visit to their laboratories and observe for yourself their installation, activities, and working relationships.

INTERNATIONAL CENTERS ON MEDICAL RESEARCH AND TRAINING

The only other item I would like to speak about is the ICMRT's which are the International Centers on Medical Research and Training. This, you will probably recall, is an effort to implement Public Law 86–610, which has two purposes.

First, to advance the status of the health sciences in the United States and thereby the health of the American people through cooperative endeavors with other countries in health research and research training.

Secondly, to advance the international status of the health sciences through cooperative enterprises in health research, research planning, and research training.

Five million dollars was appropriated for the support of this activity and the funds thus made available were distributed by Congress to the six Institutes and the Division of General Medical Sciences at the National Institutes of Health.

It was quickly apparent that although the separate Councils and Institutes could administer many aspects of the program, the international centers required a central administrative locus. Therefore, the Director of the NIH assigned the Program for International Centers for Medical Research and Training temporarily to the National Institute of Allergy and Infectious Diseases. The six councils concerned passed resolutions affirming the following policies and procedures:

1. Establishment of the need for central review and advice to the Surgeon General.
2. Identification of a portion of the International Health Act funds for support of the ICMRT program to be administered by the NIAID.
3. Approval by the Surgeon General of the International Centers applications recommended by the National Advisory Allergy and Infectious Diseases Council.
4. Incorporation of grants in the formal minutes of the other councils will constitute formal endorsement by these councils.
5. Regular progress and status reports will be made by the NIAID to the councils concerned.

The National Advisory Allergy and Infectious Disease Council, in its meeting November 20–21, 1960, concurred in these recommendations, and formally accepted the responsibility for review and conditions requested by the other councils.

To advise on program policy, criteria, and procedures, an Advisory Committee on International Centers has been appointed. The membership represents the categorical disease interests of each of the councils and each member has distinguished himself in international health circles.

An additional delegation to this committee is the periodic review of the center programs approved and funded; also, a continuing evaluation of center activities and projects. It is proposed this will be achieved through visits of committee members to the centers and periodic meetings of grantees with the committee. The first such meeting is scheduled for May 24–25, 1961. This will enable the NIAID to provide all the interested councils a detailed report at their June meetings.

The first progress report made to the councils is available. It lists the membership of the advisory committee, and gives a brief résumé of the status of each grant and its achievement as of February 27, 1961.

We have at present four approved grants. These have been made to the University of California, Tulane University, Johns Hopkins University, and the University of Maryland. Each of these sponsoring universities has one or more affiliated institutions overseas:

The University of California with the University of Malaya at Singapore, and the Institute for Medical Research at Kuala Lumpur.

Tulane University with the Universidad del Valle, Cali, Colombia, South America.

Johns Hopkins University, Calcutta School of Tropical Medicine, and the All-India Institute of Hygiene, Calcutta, India.

University of Maryland, Lahore, Pakistan.

1962 BUDGET

Mr. Fogarty. The 1961 appropriation adjusted for comparative transfers is $43,150,000. The Eisenhower budget is $44,285,000, or an increase of $1,135,000. The budget amendment adds $4,037,000, for a total increase of $5,172,000.

Will you supply for the record the history of your 1962 request?

(The information to be supplied follows:)

Development of 1962 budget estimates for allergy and infectious disease activities

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revised submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$43,344	−$8,505	$34,839	−$1,558	$33,281	−$5,207	$28,074	$35,217	$3,580	$31,637
Fellowships	2,850	−1,250	1,600	0	1,600	−200	1,400	1,600	200	1,400
Training	8,125	−2,835	5,290	0	5,290	0	5,290	5,290	0	5,290
State control programs	0	0	0	0	0	0	0	0	0	0
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	54,319	−12,590	41,729	−1,558	40,171	−5,407	34,764	42,107	3,780	38,327
Direct operations:										
Research	9,309	−156	9,153	−97	9,056	−358	8,698	8,978	0	8,978
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	655	−59	596	+10	606	−10	596	853	80	773
Training activities	0	0	0	0	0	0	0	0	0	0
Professional and technical assistance	0	0	0	0	0	0	0	0	0	0
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	243	−13	230	0	230	−3	227	244	0	244
Total direct operations	10,207	−228	9,979	−87	9,892	−371	9,521	10,075	80	9,995
Total obligations	64,526	−12,818	51,708	−1,645	50,063	−5,778	44,285	52,182	3,860	48,322

Mr. FOGARTY. For the discussion, now, give me what you first requested.

Dr. SHANNON. $64,526,000.

Mr. FOGARTY. You really got a cut.

Dr. ANDREWS. Yes, sir.

Mr. FOGARTY. What percentage is that cut?

Dr. ANDREWS. Thirty percent.

Mr. FOGARTY. What have they against you?

Dr. ANDREWS. I cannot imagine.

Mr. FOGARTY. Do you still think you can use the $64 million?

Dr. ANDREWS. Yes, sir.

Mr. FOGARTY. Will you supply for the record how you would use it?

(The information supplied follows:)

THE $64 MILLION DOLLAR BUDGET—HOW IT WOULD BE EXPENDED

The $64,526,000 would be utilized in 1962 as follows:

Grants: Research, $43,344,000; fellowships, $2,850,000; training, $8,125,000.

Direct operations: Research, 700 positions and $9,309,000; review and approval of grants, 27 positions and $655,000; administration, 16 positions and $243,000.

Total: 743 positions and $64,526,000.

GRANTS

Research.—This estimate would provide an additional $11,707,000 over the 1962 revised estimate. The projected increase of research grant funds would provide accelerated growth and permit stimulation of several areas of special interest. In the field of staphylococcal disease, added support would be given to work on a number of vexing but fundamental problems relating to virulence and communicability of the organisms, their resistance to most antibiotics, the role of "health carriers", hospital design, ultraviolet radiation, housekeeping practices, and other factors in the spread of hospital-acquired infections. Urinary tract infections and the role of the enteroviruses as causes of intestinal disease would receive vigorous investigation.

Fellowships.—Additional fellowship funds of $1,450,000 over the 1962 revised estimate would permit an expansion of support by increasing the number of qualified investigators that could be trained. Training at successively higher levels is required to keep investigators space of their fields.

Training.—The additional increase would provide $2,835,000 over the 1962 revised estimate in the training grants activity. Immunology and infectious disease, the two large areas served by the Institute's training grant program, are fundamental to many fields of health-related research. Because of this, trainees working in these programs often undertake research not only in problems of allergy and infection but also in fields supported by other Institutes and other agencies. Investigators trained under the Institute's training grant program, now in its third year, are beginning to assume academic positions and thus swell the number of available qualified teachers. Additional funds would permit these and other competent mentors to produce additional numbers of highly trained scientists to meet the growing needs for research workers and teachers (*a*) in allergic and infectious diseases and (*b*) in all other areas of medical investigation which require knowledge of infectious and allergic processes.

DIRECT OPERATIONS

Research.—The increase of approximately $331,000 for direct research included in the above would be used to expand work in parasite chemotherapy ($55,000) and upper respiratory virus studies ($65,000) and would give added impetus to the Institute's current program of acquiring and modernizing instrumentation ($94,000); $117,000 would provide additional funds for payment to the National Institutes of Health management fund for centrally furnished services.

Mr. FOGARTY. The justifications show a reserve for contingencies of $714,300. Is that all going to be used?

Dr. Andrews. It has been requested to be restored to us, and it will be used.

BACKLOG OF APPROVED GRANT APPLICATIONS

Mr. Fogarty. What will be the total of approved but unfinanced research grant applications at the end of 1961?

Mr. Kelly. If there were no institutional grants made in 1961, and if the Bureau of the Budget approved our request for release of unprogramed funds, it would be $918,050.

Mr. Fogarty. Do you think there will be any at the end of 1962 if you get only the amount in this budget?

Dr. Andrews. If we get only the amount in the Kennedy budget, we will not break even.

Mr. Fogarty. What is the estimate of approved applications you will not be able to finance?

Dr. Andrews. $5,687,000, if we initiate the institutional research grant program in 1962, and $4,167,900 if we do not.

VACCINES FOR TB AND OTHER DISEASES

Mr. Fogarty. You have been working on a tuberculosis vaccine for some time. Last year we said in our report you ought to spend more time and effort on it. What progress has been made?

Dr. Andrews. The action we have taken is to support nearly $550,000 worth of grants, about half of our total research grants for tuberculosis research, for the support of some 25 projects related to the development of more effective and safer antituberculosis vaccines.

Mr. Fogarty. Is this any more than you were doing the previous year?

Dr. Andrews. I could not tell you without looking back at the record.

Mr. Fogarty. Supply that for the record.

(The information supplied follows:)

Research grants for tuberculosis as of Jan. 1, 1961

Fiscal year	Research		Vaccine		Total	
	Number	Amount	Number	Amount	Number	Amount
1957	27	$326,666	7	$171,572	34	$498,238
1958	38	462,114	10	240,068	48	702,182
1959	35	388,467	18	372,203	53	760,670
1960	35	421,603	27	559,823	62	981,426
1961	43	588,555	25	506,502	68	1,095,057

Mr. Fogarty. What other vaccines are you working on?

Dr. Andrews. We have been working on vaccines for a number of the common respiratory viruses. I must say they have not proven to be very successful thus far. We can produce antibodies in experimental animals, but children which have been immunized, or injected with these vaccines do not have as good protection as we would hope.

I think this is a subject which is going to require a great deal of experimentation in the future, but one we are preparing to undertake.

Mr. Fogarty. Any other vaccines?

Dr. ANDREWS. We are concerned, of course, with the measles vaccines that have been prepared by some of our grantees, and are being tested by other grantees.

Then we have tularemia vaccine, and brucellosis vaccine, Colorado tick fever vaccine, and influenza vaccine, all of which have been objects of research the past year, live polio.

PROGRAM FOR TROPICAL MEDICINE

Mr. FOGARTY. How much are you spending in the tropical medicine area, and why do you consider this so important?

Dr. ANDREWS. I can supply this for the record.

Mr. FOGARTY. Supply it for the record.

Dr. ANDREWS. I prefer to do that if I may.

(The information supplied follows:)

RESEARCH ON TROPICAL DISEASES

Many of the diseases which comprise tropical medicine are not limited to the tropics, but are more easily studied there than in the subtropics or any geographically circumscribed area of the world. Certain of our temperate-zone diseases, e.g., the arthropod-borne encephalitides, are extensions of infections and parasitisms which are indigenous to the tropics but which are repeatedly introduced into both the temperate zones by migratory birds, plane-carried arthropods, and human travelers.

In a world of increasing interdependence, the health and welfare of each of us is the real and personal concern of all. Each year more of our citizens work and travel for business or pleasure to the far corners of the globe. Increasingly, the United States is host to visitors from all over the world. In an age of jet travel, communicable disease cannot be restricted to narrow geographic boundaries. Tropical diseases are a significant segment of this problem.

Economic considerations are of extreme importance. The United States obtains raw materials in great quantities from tropical areas. This will continue, as will the expansion of investments abroad. It is obvious that disease which affects the health and well-being of those in tropical areas affects the supply and the cost of imports from those countries. The minerals, nonferrous metals, mineral fuels, and other raw materials which we use in our expanding economy come in large measure from the tropics.

Billions of American dollars are invested in Latin America, the Middle East, and Africa. Here the parasitic and arthropod-borne diseases take their heaviest toll. We cannot assure our supply of raw materials by investment of money alone but must provide basic assistance in public health and education which can result in improved overall conditions. Medical research into disease problems of these areas has brought and will continue to bring incalculable dividends not alone in increased productivity but in the good relations which are immeasurable in an interdependent world.

In our present era of uneasy peace, tropical diseases continue to have important military aspects. Protection of the health of American troops and their families stationed abroad is a prime responsibility of military medicine.

Much of World War II was fought in the tropics and it is not unlikely that future military engagements may be similarly sited. Historically, disease rather than military might has been the decisive factor in victory or defeat on these battlefields. To increase medical intelligence for peace and war, this Institute is supporting, together with the Armed Forces and the Rockefeller Foundation, a survey of health research needs in the tropics which is being conducted by the National Academy of Sciences. For the same reasons, we are also heavily involved in direct and grant-supported studies of disease in the tropics.

The scope of tropical disease research at the National Institutes of Health represents a unique national resource which must be conserved and wisely used if the United States is to continue to supply tropical medicine leadership throughout the world.

The estimated amount for 1961 for research on tropical diseases is $8,900,000 of which $1,300,000 is in direct operations and $7,600,000 in the grants area.

MIDDLE AMERICA RESEARCH UNIT

Mr. FOGARTY. How much did the Middle America Research Unit spend in 1960 and how much is budgeted for 1961 and 1962?

Dr. ANDREWS. I can supply the figures for the record.

(The information supplied follows:)

1960 actual: 27 positions and $325,598.
1961 budgeted: 37 positions and $250,000.
1962 revised estimate: 43 positions and $325,400.

Mr. FOGARTY. Tell us about the housing facilities down there?

Dr. ANDREWS. The civilian people are in a very difficult situation. A request for funds for the construction of quarters has been made.

Mr. FOGARTY. How many units?

Mr. PORTERFIELD. $400,000, for 12 units of housing.

Mr. FOGARTY. What did you ask for?

Dr. ANDREWS. That is what we asked for, I believe.

Mr. FOGARTY. I wish you would also supply for the record a more detailed report on this program.

Dr. ANDREWS. Yes, sir.

(The information requested follows:)

Middle America Research Unit

The Middle America Research Unit, a field station of the National Institute of Allergy and Infectious Diseases, has now been in operation in the Panama Canal Zone for 3 full years. Jointly sponsored by the Public Health Service and the Walter Reed Army Institute of Research, the Unit emphasizes research in two major disease areas, arthropod-borne viral diseases and the fungal disease, histoplasmosis, problems for which the Panama Canal Zone setting is uniquely apt.

Both the virus and mycology laboratories have been designed to make effective use of a wide range of modern research and diagnostic techniques. In this respect alone, MARU is a facility without peer elsewhere in the Americas, outside of the United States and Canada.

In the existing MARU building, construction is underway which will result in a functioning virus research area more than twice the size of present available workspace. This will contain new isolation cubicles as well as air-conditioned desk space near the working areas of individual investigators.

Originally planned as a 3-year field research party, MARU is now a permanent laboratory facility. Recommendations by a distinguished ad hoc committee of scientists were made to accord permanent status to the Unit in recognition of the excellence of its program and its continuing potential for adding significantly to knowledge of tropical disease problems from the special vantage point of physical location in the American tropics.

With permanent status, the Middle America Research Unit may be expected to intensify and augment the present virus and mycology work of the Unit; and as opportunities arise, the group will explore new tropical disease problems of this militarily and economically strategic Central American region.

Sharing this special environment is the Gorgas Memorial Laboratory, research component of the Gorgas Memorial Institute of Tropical and Preventive Medicine. Physically located in the Republic of Panama, the Laboratory has made solid research contributions in its investigations of yellow fever, leishmaniasis, American trypanosomiasis, and malaria during the more than 30 years of its existence.

Both the Middle America Research Unit and the Gorgas Memorial Laboratory share the common objective of adding to knowledge of tropical diseases. To this end they are maintaining a close collaborative and cooperative relationship—a relationship which serves to strengthen the complementary nature of their programs. Each is the stronger for the proximity of the other, and these close ties continue to be materially beneficial.

In addition to specific projects planned as collaborative research to which each is contributing special skills and competency, mutual benefit has accrued to each group in other ways. In all the field activities of MARU which take its staff physically into the Republic of Panama, tasks are facilitated by the acknowledged status of the MARU scientists as staff associates of the Gorgas Memorial Laboratory.

In its turn, MARU has shared its facilities with Gorgas scientists and has provided specialized training in a wide range of methods and techniques. Arrangements have been made for the new virologist who will join the Gorgas staff to share the virus facilities of MARU. Through MARU, Gorgas personnel maintain close personal contact with the broadly based research program of the National Institutes of Health. After completion of new and enlarged laboratory facilities, authorized last year by a special congressional appropriation, the Gorgas group will have a modern research plant unparalleled in the tropics. Under present cooperative relationships, this will be tremendously useful in forwarding the scientific objectives of both the Gorgas Laboratory and MARU.

VIRUS ISOLATES FROM PANAMANIAN ARTHROPODS

During the first 12 months of a 3-year collaborative project on the ecology of arthropod-borne viruses in a tropical rain forest, major emphasis has been on virus isolation from various insects. Fourteen virus strains were isolated at MARU from 412 pools and 63,000 specimens provided by Gorgas scientists. Viruses were isolated from 1 per 700 *Phlebotomus* sandflies, and 1 per 7,000 mosquitoes, although rates varies greatly with species. Of the five sandfly isolates, two of broad host range (including cell culture) and short incubation period are serologically identical. These have now been identified as the Indiana type of vesicular stomatitis virus, an agent which causes disease in livestock. Because vesicular stomatitis produces symptoms which closely resemble those of hoof-and-mouth disease of animals, and must be carefully differentiated from it, the disease is a major economic problem in cattle and in horses in Panama. To some extent, it is a similar problem in the United States as well. The relationships of the other three *Phlebotomus* and nine mosquito viruses isolated are being studied with reference to each other, to known groups of other viruses, and to human and animal infection and disease.

A new approach to the problem of maintenance and transmission of animal viruses, initiated in the last part of the year, concerns the first serious attempt to explore the possible role of chiggers and related arthropods of the American tropics in transmitting disease to man. It is hoped that knowledge gained from this 2-year project will supply much-needed information concerning the role of chiggers and mites in the spread and maintenance of viruses in nature.

EASTERN EQUINE ENCEPHALOMYELITIS

Eastern equine encephalomyelitis, an arthropod-borne virus disease notable for its high fatality rate, breaks out sporadically in the United States. An example is the epidemic on the east coast of this country in 1959. In Panama, evidence suggested that this disease might be found in two particular areas and a study has been done on the prevalence of antibodies to this virus in man and in horses in those locations. In 460 humans tested, it was found that the incidence of EEE antibodies increased with advancing age from 0.8 percent in persons under 10 years of age to 9 percent in the 41–50-year group. Serologic test on the same blood specimens indicated the probable presence of other group A viruses. The relative usefulness of several serologic methods applicable to studies of this kind is now being evaluated.

Lizards of species common to these sections of Panama were examined as possible virus reservoirs, and specific antibody responses to EEE virus were noted in some of their sera.

ETIOLOGY OF JUNGLE FEVER

Some 200 paired specimens of sera were collected from military students participating in jungle warfare training courses in the Canal Zone. From one of these obtained during an episode of fever following exposure to jungle environment, a virus was isolated which had not been related to viruses known to be active on the Isthmus of Panama.

ENCEPHALOMYOCARDITIS VIRUS INFECTION

Last year scientists working at MARU described an outbreak of a fatal disease of swine caused by encephalomyocarditis virus. This was believed to be the first association of this virus with domestic animal disease. This virus can also infect man. In the animals which died during the outbreak, the outstanding lesion was acute myocarditis, an inflammation of the heart muscle. Investigation suggested that natural infection resulted from contaminated food, and experiments were undertaken in an effort to reproduce the disease by feeding virus to young pigs. Viral infection and excretion from the gastsrointestinal tract were found to occur when material infected with the virus was inoculated into the test animals. They developed high antibody levels during convalescence and at autopsy showed evidence of heart damage.

Other studies included the demonstration of antibodies to this virus in a small number of rats caught near the city and on the affected farm. Wild rodents, however, were found to be negative.

Human sera were examined with interesting differences in viral incidence, depending on the ages of donors. While a substantial proportion of the Panamanian population had been infected with EMC virus, antibodies were found more commonly in younger persons.

VIRAL FLORA OF INTESTINAL TRACT

The enterovirus flora of infants at an outpatient clinic in Panama City was systematically explored for a period of 12 months to establish a baseline of enterovirus occurrence. The majority of viruses isolated from the intestinal tract of these children belonged to the ECHO group, although in late 1959 and early 1960 poliovirus type 2 was very prevalent. This was reflected in the uncommon manifestation of a small outbreak of paralytic disease due to that virus.

Three other enteroviral studies of note are (1) surveillance for the presence of type 1 poliovirus in Panama in late 1960 as an indication of the dissemination and threatened spread of this commonly epidemic type: (2) studies of a major epidemic of ECHO–9 virus which swept through the Republic of Panama and the Canal Zone; and (3) initiation of collaborative project in children of Guatemala to explore possible relation of enteroviral flora to diet.

ARTHROPODBORNE VIRUS SECTION, BETHESDA

At the Bethesda laboratories, where the Arthropodborne Virus Section of the Laboratory of Tropical Virology is located, and of which MARU is also a part, investigators are continuing to obtain and stock both viruses and their diagnostic reagents. Viral agents of particular concern in the Middle America studies are being emphasized. These include those of eastern, St. Louis, and California encephalitides, Colorado tick fever, dengue and yellow fevers, and many others. Also under continuing study is important developmental research which is hoped to produce new or modified techniques useful to MARU investigators.

One new project involves an interesting application of the technique of antiserum pool combinations to the typing of arthropodborne viruses. Another has produced data of use in the evaluation of experimentally produced EEE virus infection in horses. A third project is an attempt to develop an inactivated eastern equine encephalitis vaccine for human use. Infected horses have yielded specific antiserum which is being processed for prophylactic use in cases of human exposure to EEE virus under laboratory or natural conditions.

A laboratory accident involving one of the senior staff resulted in infection with an arthropodborne group C (Apeu) virus. This led to the first clinical-virologic study of a syndrome produced by this important and common group of viruses of the Western Hemisphere.

HISTOPLASMOSIS

The study of histoplasmosis, a fungal disease of the lungs which is frequently mistaken for tuberculosis, is the major research interest of the Walter Reed-supported Mycology Section of the Middle America Research Unit. Since the inception of this phase of the MARU program, there has been a marked local awareness of histoplasmosis in all of its clinical forms. This has been evidenced by recognition in Panama within 18 months of three disseminated cases, two fatal and one successfully treated.

Ecologic and epidemiologic studies led to isolation of *Histoplasma capsulatum* from 8 additional soil samples, bringing to 16 the total number of recent isolations of this fungus from Panamanian soil. Until the Mycology Section was established only a single positive soil sample had been recorded in Panama. The fungus also has been repeatedly recovered from the organs of trapped ground mammals, confirming its wide dissemination in nature.

Histoplasmin skin testing continues to be the major tool for the study of histoplasmosis. Epidemiologic data on 9,200 children between 6 and 19 years of age have been obtained. As expected, the percentage of reactors to this test increases progressively with age. The rate of histoplasmin sensitivity varied from 13 to 58 percent among 6-year-olds and from 68 to 92 percent among 19-year-olds, depending on where they lived. A survey in the Canal Zone of 631 preschool children (6 months to 6 years) demonstrated an increase in hypersensitivity beginning at age 3. A similar study of Panamanian children in a city hospital is now in progress, with over 800 already surveyed.

Projects on other fungal diseases have included diagnostic study and therapy of moniliasis, a major superficial mycosis among both indigenous and transient populations in the tropics.

SHINGLES

Mr. FOGARTY. Are you doing any research on shingles?

Dr. ANDREWS. No, sir, we have no research on shingle viruses at all.

Mr. FOGARTY. Why not? They are pretty painful.

Dr. ANDREWS. Yes, indeed.

Mr. FOGARTY. Every once in a while I talk to someone who has had them and all the doctor can do is just say "Let's see how it is in 6 weeks."

Dr. SHANNON. It is self-terminating usually, in a period of about 2 months, and usually will not recur, though sometimes it has acute exacerbation before it goes. This is a disease that was studied at a fairly low rate of study, but when the cancer field opened up, and the possibility of developing new vaccines for the remedy of some of the more serious viral diseases came about, this tended to siphon off the people who had these techniques and apply them to problems they considered more urgent.

I think Dr. Andrews' estimate is correct, essentially nobody is studying this at the present time. Some people do have a continuing interest in it.

There are people who are studying the herpes viruses. There are certain other aspects of the virus that have nothing to do with the production of herpes. This is a virus that has the capability of persisting in the human body for many years, and only occasionally flaring up and giving a disease. This, you may recall, was discussed very briefly when the neurology appropriation was presented as the subject of intense investigation by the people interested in the possible viral causation of the central nervous system illness, because again, if these illnesses are the result of continued long-term residence of viruses in the body, then ups and downs would reflect periods of activity and inactivity comparable to that we see with the ordinary herpes virus, so this type of virus is of a broad continuing interest, and of increasing interest in the field of neurological disease. But when it comes to shingles, I would say there is very little activity in that particular area.

Mr. FOGARTY. Some people who have it will be very disappointed to read that. They say you do not know what it is unless you have it yourself.

Dr. SHANNON. They have one consolation, they will not have it again.

Mr. FOGARTY. You would not want it just for the satisfaction of knowing you wouldn't have it again.

Dr. SHANNON. No, sir. It is a very painful experience.

INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING

Mr. FOGARTY. Where are these international centers for medical research and training?

Dr. ANDREWS. The sponsoring universities in this country are in California, Maryland, and Louisiana.

Mr. FOGARTY. How did they become the sponsoring universities?

Dr. ANDREWS. They apply for grants to develop and support these centers, much as research grants are applied for and are made on the recommendation of expert advisory groups. Their application for grants to support this international research and training are considered by a special advisory committee.

Mr. FOGARTY. Just what is an international center?

Dr. ANDREWS. A center for medical research and training that involves more than one nationality in its operation. The sponsoring agencies are American universities; the affiliated ones are located in other countries. It is presumed that their activities, training, research planning, will be carried on at both the sponsoring university and the affiliated university.

Mr. FOGARTY. Is that the way this was supposed to work out?

Dr. SHANNON. I think there are certain aspects of this program that make the need for these centers more pointed. These involve a commitment on the part of the university concerned to support a number of scientific disciplines on broad problems of consequence to tropical areas, with perhaps some application at home, but more important——

Mr. FOGARTY. Why do you say tropical areas?

Dr. SHANNON. Well, the ones we have started so far have their field stations in what are generally called tropical belts. We are interested in them not because they are tropical, but because there are population groups in these areas that are fairly cohesive. They have certain marked differences in disease susceptibility compared to some of our own population groups. There are certain problems in common, however, relative to the infectious agents available, certain nutritional problems and certain infectious problems that are more characteristic of this tropical belt around the world.

Mr. FOGARTY. You better give me a complete breakdown of how much the grants have been to these universities, and what areas they are working in.

Dr. SHANNON. Yes.

(The information requested follows:)

INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING

The program of international centers for medical research and training was developed in response to the objectives outlined by the Congress under the International Health Research Act of 1960 (Public Law 86–610) for establishing a program through the U.S. universities for the early development of research and research training centers with adequate field opportunities for international studies. Administrative planning and support for this program during the developmental phase is being provided by the National Institute of Allergy and Infectious Diseases for the five other Institutes and the Division of General Medical Sciences who are contributing to its support.

Grants totaling $1.5 million have been awarded in fisical year 1961 to the University of California ($189,674), Tulane ($267,766), Johns Hopkins ($329,883). and the University of Maryland ($674,171), with continued support provided for 3 additional years.

The proposed plans for the international centers are comprehensive and would provide, in addition to the primary research objectives, training of medical personnel in the United States and overseas. Research projects initially will be demographic, epidemiologic and anthropometric in character in order to define the population to be used for future investigations. Specific program plans include studies on tuberculosis, histoplasmosis, and maternal and child health at the Tulane center in collaboration with the Universidad del Valle in Cali, Colombia; University of California (Hooper Foundation) and the Institute for Medical Research, Kuala Lumpur, Malaya, on insect-borne virus diseases and mycotic (fungal) diseases; enteric (intestinal) disease study by the University of Maryland and the Institute of Hygiene, Lahore, Pakistan; and hematologic and nutritional studies by Johns Hopkins and the All-India Institute of Hygiene, Calcutta.

In addition, research training will be emphasized in the fields of endocrinology-metabolism, biochemistry-immunology, cardiology, oncology, microbiology-virology, geographic pathology, and medical ecology.

Dr. SHANNON. I think the main thing here is they will provide stable institutional support for really long-term studies in these areas that has not been possible by our ordinary project grant mechanism up to the present time.

In addition, they will provide permanence of staff for career development in these areas, and we can then undertake quite a different type of research that has very definite——

USE OF POSSIBLE INCREASES IN THE 1962 APPROPRIATION

Mr. FOGARTY. Supply the record with what you would do if you had $5 million more, $10 million more, and $15 million more, for 1962 than you are requesting for these centers.

Dr. SHANNON. Yes.

(The information supplied follows:)

THE USE OF $5, $10, OR $15 MILLION ALLOCATION FOR THE INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING PROGRAM

A total of $2.4 million was earmarked for the international centers for medical research and training program. Of this amount, $1.5 million has been awarded. Pending grant applications total $900,000. It is anticipated that several new grant applications for international centers will be received during the next few months. With the normal growth of the existing and presently planned centers, it is probable that about $5 million would be required for 1962.

If the operation of the existing centers demonstrates a sound program which fulfills the intent of the International Health Research Act, it is probable that other universities will wish to participate. However, the expansion of the program will probably experience gradual development because of the many complex problems involved in setting up large-scale activities of this nature; possibly only those institutions with long traditions of overseas collaborative research and training experience would be able to participate. Considering the problems of recruitment of competent scientific and administrative staff to operate these centers, applications from these universities will probably not be forthcoming before 1963. At that time the program could be expanded to a level of $10 million or $15 million.

DEVELOPMENT OF VIRUS-FREE ANIMALS

Mr. FOGARTY. Have you done any work in trying to develop virus-free animals?

Dr. Andrews. Yes, sir. We are concerned with that right now, and it is a very difficult objective to achieve.

Mr. Fogarty. A germ-free animal was not easy to achieve?

Dr. Andrews. It was difficult, but viruses are much more elusive than bacteria and parasites, and it will be even harder to develop and maintain virus-free animals, I am sure. It is important to be able to produce completely germ- and virus-free animals if we possibly can. So far, I am not sure that we have virus-free animals.

Mr. Fogarty. You are not doing a lot on it, are you?

Dr. Andrews. Well, sir, I do not know what you mean by "a lot."

Mr. Fogarty. You have not done a great deal on germ-free animals in the last couple of years?

Dr. Andrews. Yes, we have and part of the work that is on germ-free animals is concerned in trying to get virus-free strains of mice particularly.

RESEARCH FELLOWSHIPS

Mr. Fogarty. On page 59 you say, in connection with research fellowships:

> Proportionately greater emphasis will be given in the future to the three new types of fellowship grants for the support of faculty positions at various levels.

Would this be in any way aid to medical schools?

Dr. Andrews. It is primarily for research.

Mr. Fogarty. It could be said it was aid to medical schools?

Dr. Andrews. Yes, it would provide the fellows at medical schools with the means——

Mr. Fogarty. I am not finding fault with it.

Dr. Shannon. This is indirect aid.

ADEQUACY OF THE CYSTIC FIBROSIS PROGRAM

Mr. Fogarty. In 1959 Congress provided $350,000 for studies in cystic fibrosis. What are you going to spend in 1961?

Dr. Andrews. It will be about the same level. It will be about $294,000 for grants.

Mr. Fogarty. Why is that going down? Do you think you have the problem licked?

Dr. Andrews. No, I do not think we have the problem licked, but we have about exhausted the number of researchers who are interested in working on it. That is what it really amounts to.

Mr. Fogarty. Is that so?

Dr. Andrews. Yes, sir.

Mr. Fogarty. I have heard some researchers say just the opposite.

Dr. Andrews. We would like to have them make requests for grants.

Mr. Fogarty. Did you ever hear of David Crockett?

Dr. Andrews. Yes, sir; I have heard of David Crockett.

Mr. Fogarty. He tells me they could spend a lot more money in this field. I think he and Dr. McDermott may come down and testify.

Dr. Andrews. Fine.

Mr. Fogarty. He may say they can profitably use a lot more than $294,000.

Dr. Shannon. This is for a limited aspect of studies that relates to the infectious component of this disease. There is another substantial component of support in the Institute of Arthritis and Metabolic Diseases.

Mr. FOGARTY. Is that going up?

Dr. SHANNON. I would think it is probably at about the same level.

Mr. FOGARTY. I still cannot understand why this research is going down.

Dr. SHANNON. I think the original interest in cystic fibrosis when it was called to individuals' attention caused a flurry of interest of individuals who had ideas on how to approach the disease. These ideas have not panned out. They have withdrawn from the field. I think this is not infrequently the case when any field opens up.

In the Arthritis and Metabolic Disease Institute, to give you an example, here we have for the total area $103,000 in 1958, $429,000 in 1959, $535,000 in 1960, and an estimate of something in excess of a million in 1961.

Mr. FOGARTY. What about 1962?

Dr. SHANNON. I do not have those figures, Mr. Fogarty. We would be glad to furnish an estimate. I think a projection here would be that there would be substantially more than a million dollars. I do not think we could get a closer figure than that. These are much longer range studies that deal with the metabolic and genetic underpinning of the disease, and these investigators have made a long-term commitment to the study as opposed to many who would approach it as an oddity in the field of infectious diseases.

Out of these studies in the Arthritis and Metabolic Disease Institute are more likely to come the fundamental answers to the problem, if these answers are to be forthcoming, than from the Allergy and Infectious Diseases Institute.

Mr. FOGARTY. You do not think you could wisely use more than the $294,000 budgeted for 1962 for this purpose?

Dr. ANDREWS. We are concerned with only one very limited aspect of the disease; namely, the infectious one.

Mr. FOGARTY. Just that one aspect, then.

Dr. ANDREWS. This is a staphylococcal disease, and we already have a large support for staphylococcal investigations as well.

Mr. FOGARTY. You are not asking for much of an increase, even though it is one of the most serious problems. The increase you are asking for for 1962 is very small compared to the need.

Dr. ANDREWS. I think there is a limit to the extent where you can get good work done. I believe we are about reaching that as far as the infectious element of cystic fibrosis is concerned. I do not think this is true of the other elements, however.

ADEQUACY OF RESEARCH ON STAPHYLOCOCCAL INFECTIONS

Mr. FOGARTY. What about the overall problem of staphylocccal infections?

Dr. ANDREWS. I think we have had a most fortunate incident happen this year in the development of this synthetic drug.

Mr. FOGARTY. Are you satisfied with that progress?

Dr. ANDREWS. I think this is wonderful; yes, sir.

Mr. FOGARTY. Are you satisfied? You think this is the answer?

Dr. ANDREWS. No, I am not going to predict that this is the end of the staphylococcal problem by any means.

Mr. Fogarty. How can you be satisfied with this discovery if you are not satisfied that it is the answer?

Dr. Andrews. Because I do not think anybody can foresee what will happen from the standpoint of drug fastness. There has been no indication that this drug will become fast to these organisms; as long as it does not, this is real progress, in my opinion.

Mr. Fogarty. I would say it is progress but are you satisfied with the amount of progress that has been made?

Dr. Andrews. My full satisfaction with this would mean complete cure of every case. Certainly we have not reached that stage. Therefore, I am not completely satisfied.

Mr. Fogarty. Is that not the ultimate hope of all of you people in this business?

Dr. Andrews. Yes, sir.

Mr. Fogarty. I did not think you would ever be satisfied until you found the answers.

Dr. Andrews. That is right, we must not be.

POSSIBLE USE OF PUBLIC LAW 480 FUNDS FOR INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING

Mr. Fogarty. As to these international centers for medical research and training, are any Public Law 480 funds used?

Dr. Andrews. It is not planned to use 480 funds.

Mr. Fogarty. Can they be used for this purpose?

Dr. Andrews. It would be possible. It would be easier to use foreign currencies which are owned by this country. I think that possibility will probably be exhausted before we go to the more complicated one of the 480 funds.

Mr. Fogarty. Will you put into the record at this point how the university could apply and use Public Law 840 funds?

Dr. Andrews. Yes, sir.

(The information follows:)

Use of Public Law 480 Funds in the International Centers for Medical Research and Training Program

Procedures have been established by the National Institutes of Health for partial payment of grants for International Centers for Medical Research and Training in U.S.-owned foreign currencies on deposit in foreign countries. Whenever possible, such funds will be substituted for dollars in the budget of the oversea research facility and payment in local currency will be made through the disbursing officer of the local U.S. Embassy or consulate to the U.S. representative.

TRAINING GRANT PROGRAM

Mr. Fogarty. You say that in 1962 graduates of the Institute's training grant program will be in sufficient number to direct the training program needed to achieve the Institute's goals. Does this mean you anticipate a reduction or an increase in training grants after 1962?

Dr. Andrews. I would be inclined to guess there would be an increase. There will be more available good trainers and undoubtedly more people to be trained by them.

Mr. Fogarty. All right, Doctor. Is there anything else you would like to say?

Dr. Andrews. No. Thank you, sir. I appreciate your interest.

ADEQUACY OF 1962 BUDGET

Mr. FOGARTY. It seems to me you have been hurt pretty badly in this budget estimate we have. You said in the beginning you ought to be spending $64 million in 1962, and they only gave you $44 million. That is a 30-percent cut. It seems to me you are one of the more important Institutes out there. Your work is important not only in getting answers to problems in the field of infections and allergic conditions but in helping the other Institutes such as cancer, where they are using results of your virus research, and heart and so on.

Dr. ANDREWS. Much of our work becomes developmental techniques, which are used by the other Institutes. This is true of immunology, it is true of almost all of microbiology because, whether dealing with heart disease, neurologic disease, mental disease, it becomes necessary to use the techniques of these other specialties developed for dealing with infections and allergic disorders.

Mr. FOGARTY. I cannot understand why you were cut so much.

Dr. ANDREWS. I have no explanation.

Mr. FOGARTY. Do you have anthing to say, Dr. Shannon?

Dr. SHANNON. No, sir.

Mr. FOGARTY. Do you not think this is a very important Institute? Its importance seems to be growing, from the testimony we have heard in the last week or 10 days from the Institute Directors, you and the Surgeon General. I would think you would be encouraging them instead of discouraging them like you are with this kind of budget.

Dr. SHANNON. We did not think our judgment was particularly discouraging.

Mr. FOGARTY. It does not look very good to me. It does not look like very good progress. I think you are making some pregress, but it is not as fast as I would like to see it. I do not think it is as fast as you would like to see it, either.

Is there anything else you would like to say?

Dr. ANDREWS. No, sir.

Mr. FOGARTY. Thank you very much.

Dr. ANDREWS. Thank you, sir.

INCIDENCE AND COSTS OF ALLERGIC AND INFECTIOUS DISEASES

Mr. FOGARTY. Of course, we will place in the record your statements on incidence and cost and highlights of your research.

(The statements referred to follow:)

ALLERGY AND INFECTIOUS DISEASES ACTIVITIES

MORTALITY, MORBIDITY, AND COST TO THE NATION OF THE ALLERGIC, INFECTIOUS AND PARASITIC DISEASES

Table I presents statistics on the reported deaths attributable to allergic, infectious and parasitic diseases for 1958, the last year for which national statistics have been published. Table I also presents data on the number of cases reported during 1959 and 1960 for these diseases. It should be emphasized that these figures reflect only reported deaths and cases. The figures undoubtedly are too low, since reporting is required by all States for only a few infectious diseases. Furthermore, only those deaths and cases are reported which are diagnosed by a reporting laboratory or a qualified physician, health officer, or other professional person. The inadequacies of reports on mortality and morbidity already have been documented in a special report, "The Status of World Health in Outline

Text and Chart," prepared for the Committee on Government Operations, U.S. Senate, March 10, 1959.

Data regarding certain specific diseases of interest to the National Institute of Allergy and Infectious Diseases are not available. Of particular interest in this connection are staphylococcal infections, which are distributed among several of the entries in table I, particularly "septicemia and pyemia," and "infections of the kidney," "infections of the newborn," and "infections of the skin."

Table II presents estimates of the incidence (number of cases per year), associated disability, and cost to the Nation for the allergic, infectious and parasitic diseases. Figures for the annual cost to the Nation include only the value of time lost from work due to disability. Statistics are not available to indicate the cost of medical and hospital care, drugs, and compensation specifically attributable to these diseases.

TABLE I.—*Allergic, infectious, and parasitic diseases—Reported deaths in the United States, 1958 and reported cases in the United States, 1959 and 1960*

[Data from various publications of the National Office of Vital Statistics: Vital Statistics of the United States, 1958, vol. II; Morbidity and Mortality Weekly Report, vol. 9, No. 52, January 6, 1961; Morbidity and Mortality Weekly Report, Annual Supplement: Reported Incidence of Notifiable Diseases in the United States, 1959, vol. 8, No. 53, September 16, 1960]

	Reported deaths, 1958[1]	Reported cases, 1959	Reported cases, 1960
Allergic diseases:			
Asthma	5,035		
Other allergic disorders	99		
Infectious and parasitic diseases:			
Bacterial diseases:			
Scarlet fever and streptococcal sore throat	139	334,924	308,070
Septicemia and pyemia	1,663		
Tuberculosis	12,361	78,343	
Venereal diseases	3,507	367,569	
Viral diseases:			
Acute upper respiratory infections (includes "common cold")	936		
Influenza	4,442	222,257	
Hepatitis, infectious and serum	897	24,110	41,013
Measles	552	413,156	436,379
Poliomyelitis, acute	402	8,449	3,277

TABLE 2.—*Allergic, infectious, and parasitic diseases—Number of cases, associated disability, and cost to the Nation for the period July 1, 1958, to June 30, 1959 (unless otherwise noted)*

[Data (unless otherwise noted) from various issues of the series "Health Statistics From the U.S. National Health Survey," Division of Public Health Methods, Public Health Service]

	Number of cases	Restricted activity (days)	Bed disability (days)	Work loss (days)	School loss (days)	Average daily number of persons with restricted activity	Annual cost to the Nation [1]
Upper respiratory conditions: Common cold, sinusitis, pharyngitis, tonsillitis, laryngitis, tracheitis	142,381,000	393,722,000	156,109,000	39,461,000	64,284,000	1,078,690	$685,674,000
Other respiratory conditions: Influenza, pneumonia, bronchitis (acute), pneumoconiasis, emphysema	72,966,000	306,349,000	169,915,000	39,777,000	46,390,000	839,312	691,165,000
Other infectious and parasitic diseases:							
Acute conditions	44,240,000	203,719,000	90,770,000	17,841,000	49,255,000	558,134	310,005,000
Chronic conditions (includes tuberculosis)[2]		33,300,000	16,000,000	4,600,000	800,000	91,233	79,930,000
Allergic diseases:							
Asthma and hay fever		[2] 96,553,000	[2] 30,022,000	[3] 31,000,000		[2] 264,529	[3] 538,656,000
Other allergic disorders		[3] 28,560,000		[3] 11,000,000		[3] 78,247	[3] 191,136,000
Total	259,587,000	1,062,203,000	462,816,000	143,679,000	160,729,000	2,910,145	2,496,566,000

[1] Includes only value of time lost from work, calculated on the Department of Commerce estimate of $4,344 average annual earning per full time equivalent employee, and on a 40-hour workweek, 50 weeks per year.

[2] For the period July 1, 1957 to June 30, 1958. More recent data not yet published.

[3] Nachtigall, H. B., "Compensatory Medicine," 9:5, 1957; and "Health in California," Department of Public Health, State of California, 1957. Both reflect surveys made before 1957. More recent data are not available.

HIGHLIGHTS OF PROGRESS IN RESEARCH ON ALLERGY AND INFECTIOUS DISEASES, 1960

Items of interest on program developments and research studies conducted and supported by the National Institute of Allergy and Infectious Diseases

VIRUS DISEASES

Vaccine against measles promises immunity comparable to natural disease

Impressive evidence of effectiveness of an experimental virus vaccine for measles is presented in eight consecutive reports in the New England Journal of Medicine. These articles represent the work of 23 investigators working in 11 institutions which are receiving grant support from 7 organizations.

The investigators agree that any proposed vaccine for measles must be justified as both desirable and acceptable. In measles, because of the significant mortality, frequency of bacterial complications, occasional involvement of the central nervous system, widespread morbidity of the uncomplicated disease, heightened virulence of outbreaks in isolated populations and unfavorable effects on certain other pre-existing illnesses, a preparation conferring immunity comparable to natural measles seems desirable.

It is the consensus that the present experimental vaccine may be acceptable because of the following properties: ease of administration; lack of local reaction; absence of communicability; high index of serologic response; elimination of bacterial complications; and prophylactic efficacy demonstrated under the circumstances described.

The magnitude of the measles problem is indicated by the following statistics. In 1958, the last year for which complete figures are available, 552 deaths in the United States were attributed to measles in contrast to 255 for poliomyelitis. A dreaded complication of measles is encephalitis, reportedly ranging in incidence from 1:400 to 1:1000 cases. With an attack rate of 70 to 95 percent among persons susceptible to measles and with a U.S. birth rate of 4 million annually, the morbidity of uncomplicated disease alone is immense and the proportion liable to severe complications considerable.

The work on the vaccine supported by the National Institute of Allergy and Infectious Diseases (articles IV and V in the series) is concerned with two aspects of the study. Drs. F. L. Black and S. R. Sheridan of Yale University School of Medicine compare the effectiveness of the subcutaneous route of injection with others that might be involved in natural transmission of measles. Drs. M. L. Lepow and F. C. Robbins, with Nigel Gray, report the clinical, antigenic and prophylactic effects in institutionalized and home-dwelling children.

Results obtained in the trial of subcutaneous vaccine, which proved superior to inoculation by other routes, were in keeping with those of other investigators: a predictable incubation period shorter than in natural measles; a roseolalike course of illness without rash and fever; no cough, coryza and conjunctivitis; surprising lack of malaise and prostration when fever was present. Production of antibodies was reliable and leukopenia was a relatively constant sign of response to the vaccine. No contact spread was seen.

In the study by investigators Lepow, Gray, and Robbins, as in the others reported, the majority of the systemic reactions were mild, according to the physicians and the parents of the study children. Fever, anorexia and lethargy were predominant features of the 15 percent of reactions considered moderate. Serologic data indicate that an adequate immune response does occur, and thus far complete protection has been demonstrated in 10 children after household exposures to the natural disease. None of the children who had detectable complement-fixing antibody in their preimmunization serum samples showed any rise in titer as a result of administration of the vaccine. Parents who had seen natural measles in other children considered the vaccine-induced reaction in the study group considerably milder.

One problem that complicated assessment of the rate and severity of the reactions to the vaccine was the presence of intercurrent infections suffered by one-fourth of the susceptible children during the 14-day postvaccination period. It is quite possible, the authors believe, that some of the respiratory symptoms attributed to vaccine resulted from other infectious agents. There was no evidence, however, that intercurrent infections interfered in any way with antibody response to the vaccine.

Parental acceptance of the vaccine will depend on an awareness by parents of the hazards attending ordinary measles as well as preparation for the expected reactions to the vaccine. Laboratory efforts are continuing in an attempt to provide an agent that may induce comparable serologic response with less febrile reaction. At this time the investigators believe it appropriate to recommend extension of clinical trails of attenuated measles-virus vaccine in special groups and a conservative extension of its use in normal children.

Twenty-eight percent of respiratory viral illness in young adults now identifiable

Among young adults at the University of Wisconsin, the measure of acute respiratory disease which can be identified etiologically has been raised to over 28 percent by Dr. Alfred S. Evans, a grantee of the National Institute of Allergy and Infectious Diseases. The report, published in the New England Journal of Medicine, evaluates the importance of the hemadsorption viruses in the total picture of respiratory disease.

Dr. Evans' achievement represents another advance in the effort to clarify the etiological problem of undifferentiated acute respiratory disease. In previous work, Dr. Evans had identified about 20 percent of these illnesses etiologically, including streptococcal infection (7 percent), influenza infection (8.7 percent), adenovirus infection (1.4 percent), and other bacterial infection (1.2 percent). Results of the present study serve to identify still another segment of the etiologic "pie" in the order of 8 to 10 percent and mark the hemadsorption viruses as the most frequent cause of sporadic respiratory infection found in the student body to date.

The scientist reported on 227 paired serums from students (age 17 to 26) hospitalized in the student infirmary with respiratory illness from January 1957 through April 1959. Cases occurred throughout the year although the periods following summer and Christmas vacations contained a greater portion of the total.

In 200 patients tested by complement-fixation for hemadsorption type 1, 8.5 percent gave evidence of infection. For hemadsorption type 2, the figures were 1.5 percent of 202 patients. In serums from 175 patients on which both tests were made, a total infection rate of 9.1 percent was obtained.

Clinical diagnoses associated with these infections included acute respiratory disease, acute pharyngitis, acute tonsillitis and pneumonitis. However, no distinctive clinical pattern permitting recognition of the cause of infection at the bedside could be detected.

Mumps virus in central nervous system may be wrongly diagnosed as paralytic polio

According to Dr. Edwin H. Lennette and cooperating scientists, working under a grant from the National Institute of Allergy and Infectious Diseases, a central nervous system involvement with mumps virus may be incorrectly diagnosed as paralytic poliomyelitis. Results of this investigation are published in Pediatrics.

Although attention has already been focused on the differentiation of disease of the central nervous system due to mumps from nonparalytic poliomyelitis, some cases are observed in which muscle weakness and paralysis occur. These cases are usually diagnosed on the basis of the simultaneous presence of parotitis and muscle weakness, or on positive serologic tests for mumps in a paralytic poliomyelitis-like syndrome. However, in previous studies, the possibility of concurrent poliomyelitis had not been ruled out.

In the current investigation the scientists observed cases of mumps virus infection in children associated with local muscle weakness resembling that of mild paralytic poliomyelitis. In all instances this weakness was still present at the time of hospital discharge; in four cases it was still detectable 2 months after discharge. All of the patients had been initially diagnosed and reported as spinal paralytic poliomyelitis.

Of the four cases displaying a residual weakness after discharge, two gave no laboratory evidence of current or past poliomyelitis virus infection. In the others, failure to recover poliomyelitis virus from the stools, together with the absence of demonstrable CF antibody, was considered strong evidence against recent infection. In each case the diagnosis of mumps infection was based on the occurrence of a fourfold or greater rise in the titer of mumps antibody during the illness.

For the seven remaining cases, a diagnostically significant rise in mumps CF antibody was shown. Again no evidence of current poliomyelitis virus infection, either by isolation of the virus or demonstration of a significant rise in CF or neutralizing antibodies, was found. While low titers of CF antibody and substantial neutralizing antibody titers against one or more types of poliomyelitis virus were present in both acute and convalescent sera from these patients, antibody levels such as these are commonly found in children who have experienced subclinical infection with poliomyelitis virus at some time in the past and have subsequently had their natural antibody "boosted" by vaccine. Thus, although the possibility of concurrent poliomyelitis is not unequivocally excluded in these latter cases, the investigators offer them as additional examples of mild paralytic illness in which the mumps virus is very likely the etiologic agent.

Viruses may be important cause of shipping fever in cattle

Parainfluenza 3, a virus closely related to a common human viral agent, has been isolated from cattle with the respiratory disease known as shipping fever, adding weight to the thesis that viruses may be an important cause of this infection.

From 1957 through 1959 in 7 separate outbreaks of respiratory disease in calves and older cattle, 13 isolations of this agent were made from nasal secretions and diseased lungs of the sick animals and from the nasal secretions of 3 apparently normal calves. The viruses were isolated on tissue culture of bovine embryonic kidney and were identified by the hemadsorption-inhibition technique. Although serological neutralization tests were done, hemagglutination inhibition was found to be equally sensitive and was therefore used extensively throughout the studies.

A report on this research appears in the American Journal of Hygiene. Coauthors are Drs. F. R. Abinanti and R. J. Huebner, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases; Drs. R. J. Byrne, L. J. Poelma, and F. R. Lucas, University of Maryland Department of Veterinary Science and the Maryland Livestock Sanitary Service at College Park; and Dr. R. L. Watson, Communicable Disease Center, Atlanta.

Prior to recovery of this virus from cattle, a closely related virus, which is apparently common in humans, was shown to be responsible for respiratory illnesses in infants and young children. In a study published last year, parainfluenza 3 virus was shown to have caused 50 percent more acute respiratory disease in hospitalized children than the virus of Asian influenza.

The authors point out that the study of respiratory disease in cattle is of great importance not only to the livestock industry, which must cope with the economic aspects of animal disease and death due to such outbreaks as shipping fever, but to those interested in human viral disease. The investigators believe that respiratory diseases in cattle can serve as useful models of respiratory disease in humans. Rates of infection and the influence of the immunological and physiological state on these rates may be studied, as may the relationship of clinical infection to clinically inapparent infection, seasonal prevalence of disease, and physical factors concerned with the spread of respiratory infections. With a bovine population it is also possible to do detailed studies on the use of vaccines, assessing their usefulness in the control of respiratory disease.

With regard to the isolation of virus from apparently normal calves, the investigators note that their current studies do not establish whether these animals became infected by exposure to cattle or to humans. Parainfluenza 3 spreads readily from person to person so that bovine or other animal sources are unnecessary to explain frequent human infections. However, the possibility that domestic animals may serve as reservoirs of common human viruses requires careful study.

Interest in the problem of respiratory disease of cattle is international. During their research, Dr. Abinanti and his coworkers in the Laboratory of Infectious Diseases have run serological tests of bovine sera not only from different parts of the United States but from Tahiti and Japan, and have demonstrated parainfluenza 3 antibody in these sera. In Sweden, investigators at the Swedish Institute of Veterinary Medicine have reported isolation of a virus identical with parainfluenza 3, which they believe might be the primary cause of so-called transport disease.

Variants resist temperatures previously thought to destroy all three polioviruses

A research team supported by an NIAID grant revealed poliovirus variants which resisted temperatures generally believed to be rapidly destructive of all three types of virus. Drs. Donald N. Medearis, Jr., John H. Arnold, and John F. Enders conclude in the Proceedings of the Society for Experimental Biology and Medicine that survival of appreciable quantities of poliovirus under the conditions imposed by their experiments makes it doubtful whether pasteurization of milk and other food products as now carried out can assure completely the inactivation of these agents.

The scientists obtained their results in a series of experiments initiated after unexpected multiplication of poliovirus type II had been encountered in safety testing of a suspension heated at 65° C. It had been intended to employ this suspension as antigen in skin tests on human beings.

Their experiments showed that suspensions of polioviruses types I, II, and III, in medium 199 derived from infected monkey kidney cell cultures, were not completely inactivated following exposure for 1 hour to temperatures of 60° C. and 65° C. In one instance infectious virus was demonstrated in a suspension of poliovirus type II after heating at 75° C. for 1 hour. Progency of virus surviving at this temperature exhibited increased thermoresistance. Acknowledging the need for supplementary experiments, the scientists say that on the basis of their findings it would seem that these highly resistant variants do not "breed true" in the sense that their progeny are equally resistant. However, mean resistance of the progency is increased. This would suggest, the scientists believe, that more than a single gene may determine, in association with environmental phenomena, thermoresistance of the progeny.

Factors to account for the difference between these results and those of previous investigators are not readily apparent. The concentration of extraneous protein in these preparations which might enhance thermostability was as low or lower than that in preparations examined by others. The pH was maintained at neutrality or slightly on the alkaline side where the stabilizing effect of cystine is not critically operative. It is possible that the higher concentrations of virus employed in these experiments together with replicate tests in a fairly large number of cell cultures of high sensitivity observed over long periods may be responsible for the discrepancy, the scientists conclude.

Complement fixation useful to confirm clinical diagnosis of Colorado tick fever

Diagnosis of Colorado tick fever by complement fixation can be accomplished routinely in most diagnostic laboratories, according to data presented by Drs. Leo A. Thomas and Carl M. Eklund of the National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Mont. This test, which is much simpler than any of those previously used, is described in the Journal of Infectious Diseases.

Previous studies from the Rocky Mountain Laboratory have shown that Colorado tick fever virus can be isolated readily from blood obtained from patients during the febrile period of their disease, either by inoculation of suckling mice or of KB tissue culture cells, and that isolation and identification of virus is the most rapid method of laboratory diagnosis. These and other research procedures, however, are not suitable for the average diagnostic laboratory.

Drs. Thomas and Eklund, using a complement-fixing antigen prepared by Casal's technique from suckling mouse brains infected with Colorado tick fever virus, found the CF test satisfactory in detecting antibodies in serums from patients convalescent from Colorado tick fever. Complement-fixing antibodies first appeared 20 days after onsent of illness, 1 week later than neutralizing antibodies, and were present in one patient for as long as 260 days.

Acute and convalescent serums were available from more than 50 patients on whom a clinical diagnosis of Colorado tick fever had been made, substantiated by isolation of virus from blood taken during the acute phase of illness and demonstration of neutralizing antibodies in blood taken during convalescence. Approximately 80 percent of those collected after the fourth week of illness contained demonstrable CF antibodies. The authors conclude that the complement fixation test can be used successfully to detect antibodies following infection with Colorado tick fever virus. They emphasize that serums for the test should be collected 4 weeks or longer following onset of illness. The test should prove of value, they believe, in general diagnostic laboratories as confirmation of the clinical diagnosis of the disease.

Studies of mouse polyoma (tumor) viruses extended by field work in New York City

The ability of the mouse polyoma virus to produce multiple tumors in mice and other rodents has aroused great interest and stimulated extensive studies of virus by many laboratories. One of the basic questions raised in relation to this virus is, "What manifestations does the polyoma virus produce as it occurs naturally?"

Drs. Wallace P. Rowe, Robert J. Huebner, and Janet W. Hartley of the National Institute of Allergy and Infectious Diseases reported at the Gustav Stern Symposium on Perspectives in Virology on studies of the natural occurrence of polyoma virus in mice (*Mus musculus*) inhabiting densely populated areas of New York City, particularly Harlem. The NIH scientists were aided in the field work by the New York City Health and Sanitation Department. Approximately 1,000 mice were studied. The natural history, the importance of ecto-parasites, the mode of spread of the virus, and the tumorigenic activity of "wild" polyoma virus strains were studied. The basic tool for these studies is the hemagglutination inhibition test, which serves both as the indicator of past infection and the end-point of sensitive virus detection tests in laboratory animals and tissue culture systems.

In the Harlem area infection was found in high frequency along certain blocks, while nearby blocks were completely negative. There was marked difference in frequency of infection of mice trapped in different apartment houses within a single block. Virus was recovered from the organs of 14 wild mice, and also twice from floor sweepings in apartments housing infected mice. Virus was isolated from the excreta of three of the mice. Mites recovered from infected mice were found negative for the virus. Cockroaches trapped in the apartments were also negative.

Excretion of virus apparently plays an important role in its transmission in nature. In laboratory experiments, infected newborn mice have been found intense sources of environmental contamination. Eating and drinking contaminated food and water appeared to be possible modes of entrance of virus into mice. However, inhalation of virus appears to be a more effective mode of entry.

The important question of the relation of polyoma virus to the occurrence of spontaneous mouse neoplasms was also discussed at the Gustav Stern Symposium by Dr. Rowe. He described studies undertaken with the collaboration of the Roscoe B. Jackson Laboratories, Bar Harbor, Maine, where large numbers of mice of various inbred strains and hybrid combinations are observed for life and autopsied when moribund from any cause. Polyoma antibody in tumorous mice was compared with that in mice dying without tumors. Among the inbred strains there was not the slightest indication of any excess of polyoma antibody among tumorous mice compared with comparable nontumorous mice. In the hybrids the situation was essentially the same.

Virus may be unnecessary to maintain tumor in vivo once tumor initiated by polyoma

Recently completed studies by Dr. Karl Habel, Chief of NIAID's Laboratory of Biology of Viruses, and his associates, on the factors responsible for the tumor-producing properties of polyoma viruses have raised a question concerning the necessity for virus presence in maintenance of the tumor. Findings were reported at the meeting of the Federation of American Societies for Experimental Biology, 1960.

Dr. Habel inoculated newborn mice and hamsters with polyoma virus to produce fibrosarcomas which were transplanted into adults of the corresponding species. In the hamster, although virus could be demonstrated in the original tumor, no further evidence for its presence could be found after the first transplant. Attempts to induce these virus-negative tumor transplants to produce virus in tissue culture under X-ray or ultraviolet radiation failed. On the other hand,in one series of mouse tumor transplants the association of virus with tumor has been consistently positive for 10 transplants.

When virus was given to newborn hamsters, along with antiviral serum at a different site of inoculation, tumors appeared after a longer incubation period. Certain of these tumors apparently were not producing virus, however, since the animals gave no evidence of harboring virus antibodies.

The investigators feel that continuing studies of this nature may help clarify tumor-producng properties in other agents and may eventually lead to better understanding of tumor development under natural conditions in man.

Encephalomyocarditis virus now implicated in animal disease as cause of death of swine

A group of scientists has for the first time described a natural infection of swine with the EMC virus. Dr. Thomas G. Murnane of the U.S. Army Mission to Panama, Drs. John E. Craighead and Alexis Shelokov of NIAID's Middle America Research Unit, and Dr. Harold Mondragon of the Gorgas Hospital, reporting in Science, believe it is the most extensive outbreak of EMC infection either in man or in animals, in which the virus has been recovered. In all cases, the investigators found severe myocarditis to be the outstanding lesion.

The outbreak of disease occurred on a commercial swine farm near Panama City where approximately 30 pigs died during a 20-day period in 1 feedlot of 300 animals. Three of the animals were examined histologically, revealing severe myocarditis with round cell infiltration, vascular congestion, edema, and degeneration of the myocardial fibers; mild pneumonitis and pulmonary edema; mild meningitis and minimal congestion of the brain with spotty areas of neuronal degeneration.

As a result of bacteriological and virological studies performed on two of the animals by the investigators, an agent pathogenic for mice was repeatedly isolated from the lung and spleen of the animals and from one of the brains. The same agent was recovered from the brain, lung, and spleen of inoculated mice.

EMC virus is also pathogenic for young hamsters and guinea pigs, and has been reisolated and passaged in cell cultures of rhesus monkey kidney, hamster kidney, and HeLa cells.

The scientists identified the agent by neutralization tests in mice and tissue culture with a hyperimmune rabbit antiserum prepared against the American-type culture prototype strain of EMC virus. Identification was confirmed at the Walter Reed Army Institute of Research.

The disease was successfully reproduced by inoculation of two young pigs with mouse-passage virus. In both animals viremia was demonstrated on the second day with the first signs of disease appearing on the third. As in the naturally infected animals, the scientists found a severe myocarditis upon sacrifice or death.

Aedes vexans *mosquito implicated in eastern equine encephalitis in Connecticut*

Supported by a grant from the National Institute of Allergy and Infectious Diseases, Dr. R. C. Wallis and associates of the Yale University School of Medicine have for the first time isolated EEE virus from the *Aedes vexans* mosquito. The report is published in the "Proceedings of the Society for Experimental Biology and Medicine."

In their study the scientists took weekly samplings of mosquitoes during the spring, summer, and early fall of 1959, at the Shade Swamp Fish and Game Wildlife Refuge in Farmington, Conn., where epidemics of EEE occur irregularly among the pheasant population. Adult female mosquitoes from these samplings were stupefied with cigarette smoke, sorted into pools by species, stored and later processed in the virus laboratory.

Of 3,194 mosquitoes collected, 70 percent were of the *Aedes cinereus* and *canadensis* species. Although *Aedes vexans* accounted for less then 5 percent of the specimens, the only virus isolation was made from a pool of 13 females of this species. Identification was made by both hemagglutination-inhibition and neutralization methods by titrating against a known EEE immune serum.

Dr. Wallis indicates that circumstantial evidence had long supported the possibility of EEE transmission by mosquitoes. In 1956, during an encephalitis epidemic in pheasants in New Jersey, four isolations of EEE virus were obtained from pools of *Culiseta melanura*, providing strong evidence that this species was a significant vector in birds. Correlation of this species' distribution with incidence of the disease could not be confirmed in Connecticut despite several studies during which, however, *A. vexans* was found repeatedly. Unlike *C. melanura*, its distribution extended to all areas where virus activity occurred. This epidemiological consideration—plus the knowledge that *A. vexans* is a vicious biting mosquito; has a wide variety in its host range, feeding readily on man, horses, cattle, and birds; enters houses and barns and attains its population peak late in the summer just prior to the EEE epidemic season in the New England States—led investigators to consider it as a probable vector. With the present isolation of the virus from *A. vexans*, this consideration has been confirmed and *A. vexans* assumes a new epidemiological significance.

Mosquitoes, viruses implicated in new human epidemic hemorrhagic fevers

Several previously recognized types of virus and others closely related—some observed for the first time—apparently have an etiologic role in a new and frequently fatal type of hemorrhagic fever occurring in the Philippine Islands and in Thailand. Drs. W. McD. Hammon, A. Rudnick, and G. E. Sather of the University of Pittsburgh have reported epidemiologic, clinical, and etiological studies on this highly lethal disease in Science. The work was supported by a grant from the National Institute of Allergy and Infectious Diseases.

The scientists reported the occurrence of approximately 3,250 cases in Manila and Bangkok, 10 percent of which were fatal. Nearly all patients were children below the age of six from areas where *Aedes aegypti* mosquitoes were present in large numbers. The clinical manifestations of the disease varied somewhat in the two locations, leading the scientists to postulate the presence of two or more related but different agents.

Mosquitoes were collected from the epidemic area and serum specimens were obtained from patients in the acute and convalescent phases of the disease. In the Manila area, 14 viruses were isolated by adaptation to suckling mice, and significant rises in antibody titer to those viruses were demonstrated in several cases in the epidemic. All of the viruses isolated during the epidemic in Manila proved to be antigenically related to dengue, types 1 and 2, but represented newly recognized viruses for the most part. These were provisionally designated as dengue, types 3 and 4.

Human sera yielded dengue virus types 2, 3, and 4, while *Aedes aegypti* and *Culex tritaeniorhynchus* yielded dengue, type 3. This was the first instance ever reported of the isolation of a dengue virus from wild-caught mosquitoes.

Of nine virus isolations from the epidemic in Bangkok, six were antigenically similar to dengue type 2, the remainder to chikungunya virus (a group A arthropod-borne virus known to cause a dengue-like febrile disease in Africa). Three viruses were isolated from *A. aegypti* and characterized as dengue, type 2, while all other dengue and chikungunya viruses were isolated from serum specimens.

Serological studies, as yet incomplete, have related infection with one or more of these viruses to the disease by demonstrating a rise of antibody titer in suitably spaced paired specimen.

In summary, although the investigators feel it is premature to associate the presence of all these agents in the blood of patients suffering from the broad clinical syndrome of hemorrhagic fever with the *A. aegypti* mosquitoes of the two epidemic urban areas, the bulk of evidence points to a probable etiologic relationship.

New virus of arthropod-borne group B isolated from Colorado ticks

From a pool of 20 ticks collected along the North Cache la Poudre River, Colo., a virus has been isolated at the Rocky Mountain Laboratory which has been shown to be closely related if not identical to Powassan virus. In 1958 Powassan virus was found in the Western Hemisphere for the first time. A group of Canadian workers isolated it from the brain of a 5-year-old boy dead of an acute encephalitis.

The isolation at the Rocky Mountain Laboratory is reported in the "Proceedings of the Society for Experimental Biology and Medicine," by Drs. Leo A. Thomas, Richard A. Kennedy, and Carl M. Eklund of the National Institute of Allergy and Infectious Diseases. Isolation in the United States of an agent related to a group of viruses known to cause extremely severe illness in other parts of the world necessitates continued studies to determine the ecological factors associated with the virus and the degree to which man is exposed to infection, the authors believe.

Ticks (*Dermacentor andersoni*) were injected into mice which then developed illness suggestive of encephalities. Serologic studies of the agent isolated from the mice included hemagglutination, hemagglutination-inhibition, complement fixation, and neutralization tests. These tests differentiated the virus from others such as Japanese B, Ilheus, Murray Valley, West Nile, St. Louis, and Russian spring-summer encephalitis viruses, but not from Powassan virus.

Scientists at the RML have studied ticks in the western United States for a number of years to determine their role in disease. Techniques suitable for isolation of the Powassan-like agent have been employed and many isolations of tick fever virus made from thousands of ticks, but until the present study there was no evidence that other viruses were present. According to the investigators, these studies suggest that some insect other than ticks may be a reservoir or vector of the virus. There have been some observations based on serologic studies that certain individuals in the Western States have antibodies against group B arthropod-borne viruses which cannot be accounted for by the agents previously known to be present in these areas.

ALLERGY—IMMUNOLOGY

Site of intracellular antigen demonstrated by fluorescence in three myxoviruses

The finding that intranuclear antigen production so prominent in the multiplication cycle of influenza and fowl plague viruses is not demonstrable in the cycle of Newcastle disease virus, Sendai, or mumps viruses is reported by Drs. Myrna I. Traver, Robert L. Northrop, and Duard L. Walker of the University of Wisconsin. The report of this work, supported partly by a grant from the National Institute of Allergy and Infectious Diseases, appears in the "Proceedings of the Society for Experimental Biology and Medicine."

Using fluorescent antibody technique, the investigators compared the multiplication cycles of NDV, Sendai, and mumps viruses with that of influenza A virus. They used antisera from three species, several multiplicities of infection, and two cell types to assure that the observed patterns of antigen development and distribution were not peculiar to a special set of materials or conditions. For examination by fluorescence microscopy cells were grown on cover glasses in tubes with flattened sides. Controls consisted of uninfected cells treated with specific conjugate, infected cells treated with normal serum, and, on certain occasions, infected cells pretreated with unlabeled antibody prior to staining with labeled antibody.

The three noninfluenza viruses (NDV, Sendai, mumps) were observed through an entire cycle of infectivity. During periods up to 26 hours, nuclei appeared consistently as clear, nonfluorescent areas; specific viral antigen was visible in the cells as granules distributed throughout the cytoplasm. A marked difference was observed with influenza virus. In this virus, antigen was first seen by fluorescence in the nucleus, followed by later appearance in the cytoplasm.

The authors emphasize that while the present study indicates that intranuclear production of antigen demonstrable by fluorescent antibody is not characteristic of the noninfluenza viruses tested, it remains possible that the nucleoprotein antigen is produced within the nucleus in a form that does not combine with antibody under the conditions of current fluorescent antibody technique. On the other hand, it may be that with these viruses antigen is produced not in the nucleus but in the cell cytoplasm. Studies are in progress to clarify this point. The demonstration that intranuclear antigen production so prominent in the multiplication cycle of influenza and fowl plague viruses is not demonstrable in the cycle of NDV, Sendai, and mumps viruses may add another characteristic to those which seem to separate the myxoviruses into two distinct subgroups.

New diagnostic procedure developed for lupus erythematosus

A simple and rapid diagnostic test for lupus erythematosus has been developed by scientists of the National Institute of Allergy and Infectious Diseases. Mr. John Bozicevich, of the Laboratory of Immunology, in cooperation with Drs. John P. Nasou and Donald E. Kayhoe, of the Laboratory of Clinical Investigation, describe the procedure as similar to the bentonite flocculation test originally devised against rheumatoid arthritis.

In this case, however, desoxyribonucleic acid (DNA) is substituted for gamma globulin as the sensitizing agent for the bentonite particles. These are added to heat-inactivated serum dilutions to effect the flocculation reaction. The results of the study are reported in the "Proceedings of the Society for Experimental Biology and Medicine."

In the clinical evaluation of the new diagnostic procedure in eight patients with lupus erythematosus, the investigators compared the results of the new flocculation test with those of the widely used lupus erythematosus cell test and found them comparable.

The scientists indicate that one of the disadvantages inherent in the L.E. cell test is the need for employing fresh whole blood. In the newly developed DNA-bentonite flocculation test only the patient's serum is required.

While it is true that cases in remission are apparently more sensitive to the older test (two out of five patients of this type yielded positive reactions to the L.E. cell test but reacted negatively to the flocculation tests) the new procedure appears to be more specific. This was indicated in tests with serum from six rheumatoid arthritis patients which gave positive reactions with the L.E. cell test and negative reactions with the flocculation procedure.

As controls, the investigators tested sera from 138 individuals, including normal subjects and those with related and unrelated diseases. The new flocculation procedure gave negative readings in each case. Ninety-four of these 138 individuals were evaluated by the L.E. cell method. Six of them reacted positively even though there was no clinical evidence of the disease.

Newborn infants shown capable of developing significant antibodies to various viruses

A recent study published in Pediatrics by Dr. Heinz Eichenwald and Olga Kotsevalov, grantees of the National Institute of Allergy and Infectious Diseases, has cast doubt on the belief that human infants do not begin to form adequate circulating antibodies to injected bacterial antigens until the second month of postnatal life.

Over a 5-year period the scientists tested more than 4,000 infants to obtain sufficient data on the 35 infants illustrating their report. Natural infections studied included those resulting from adenovirus types 1, 2, and 3 and ECHO virus types 9, 18, and 20. Standard serological techniques were employed in identifying the isolated cytopathogenic agents, and neutralizing antibody titers were determined for each patient by testing serum against the particular strain of virus isolated.

The scientists feel that their data are not sufficiently extensive to warrant many definite conclusions concerning the immunologic responsiveness of premature and young full-term infants to viral infection. Viruses are detectable in these special groups only rarely and then the interval between the time a specimen is obtained and a virus isolated may be too long to permit adequate serologic followup.

They concluded from their findings that it is impossible to generalize on the basis of experience with one virus. For example, 12 premature and 5 full-term infants infected with ECHO virus type 18 were ill with diarrhea, while 4 full-term infants (less than 8 days of age) harboring ECHO type 20 did not manifest any obvious symptoms. Yet, infection with either of these viruses apparently produces consistent antibody response. On the other hand, adenovirus type 1 infection which was not associated with any recognized illness in the 5 premature infants investigated and adenovirus type 3 (6 full-term infants ranging from 12 to 37 days of age) which may produce diarrhea in some and no disease in others, did not always produce a detectable antibody response. Despite this, the infection does not disseminate and eventually subsides. Obviously, the ability to form antibodies represents only a small part of the total host response to infection.

According to the scientists, one general fact emerged from the study: newborn and premature infants naturally infected with various types of ECHO viruses and adenoviruses usually respond promptly with antibody formation. Whether or not detectable antibodies develop is apparently closely related to the inherent antigenicity of the agent—that is, to the particular virus involved—rather than to the patient's maturity.

Relation between delayed and immediate hypersensitivity, important aspect in allergy

Laboratory experiments directed toward unraveling the relation between delayed and immediate types of hypersensitivity are in progress at the Rocky Mountain Laboratory, field station of the National Institute of Allergy and Infectious Diseases in Hamilton, Mont. Only recently has it been possible to demonstrate a relation between immediate and delayed types of sensitivity in experimental animals.

It has been suggested that delayed hypersensitivity is a step in the formation of circulating antibody. This raises the question of whether or not delayed sensitivity has a more primitive type of specificity than do Arthus reactions and circulating antibody. This is among the concepts being explored by Drs. S. B. Salvin and R. F. Smith at the Rocky Mountain Laboratory. Their first paper in a series on specificity of allergic reactions appears in the Journal of Experimental Medicine.

The investigators recognize that two contradictions may seem to invalidate the hypothesis that delayed hypersensitivity is a stage in the production of circulating antibody. First is the difficulty of producing circulating antibodies to denatured proteins, such as gelatin, although delayed hypersensitivity develops; the second, the inability to detect delayed hypersensitivity to purifed polysaccharides, although circulating antibody may occur. Both of these facts may be explained on the basis that recognition of antibody by antigen in delayed hypersensitivity is directed toward a broad area of the antigen molecule, and in Arthus reactions and circulating antibody toward a more narrow, finite area.

By employing various types of avian albumins and different conjugated proteins prepared from them, it was possible to show that the delayed reaction is produced in guinea pigs in response to a broad general area of the antigen molecule. Activities of circulating antibody, however, are directed by small, specific groupings of the antigen.

When conjugated proteins, such as picrylated hen albumin, are used as antigens for guinea pigs, the animals develop delayed reactions to the protein portion, and antibodies and immediate reaction to the haptenic portion of the complex.

Allergic encephalomyelitis demonstrated to have immunological basis

A successful transfer of allergic encephalomyelitis has been brought about by the injection of lymph node cells taken from donor rats sensitized to spinal cord into recipient rats pretreated neonatally with normal rat spleen cells. The study was undertaken at the New York University College of Medicine by Dr. Philip Y. Paterson, of the Institute's Laboratory of Immunology. Findings were published in the Journal of Experimental Medicine.

Dr. Paterson pretreated newborn rats with pooled, normal spleen cells from splenectomized adult donor rats. Five to six weeks later the donor rats were injected with guinea pig spinal cord in adjuvant. Lymph node cells were collected from the donors 7 to 12 days later. These were pooled, washed, and injected intravenously into the pretreated, and now adult, recipient rats. The recipients were observed for 6 to 8 days after lymph node cell transfer, then sacrificed, and their brains and spinal cords examined microscopically for neurological lesions. Comparable lymph node cell transfers were performed using control donors injected with guinea pig kidney-adjuvant and control recipients which were not pretreated with spleen cells.

As a result of the transfer of lymph node cells to recipient rats pretreated with spleen cells from the same donors, 14 of 22 recipients were found to have allergic encephalomyelitis lesions after injection of 10 to 156 million viable donor lymph node cells. The number of lesions demonstrable in each of these 14 positive recipients varied from a minimum of 2 to a maximum of 15 and both their number and intensity appeared to be directly related to the number of donor lymph node cells transferred.

Dr. Paterson performed additional lymph node cell transfers using recipients pretreated neonatally with spleen cells from rats other than those providing the transferred lymph cells. Of these a total of 6 of 29 recipients acquired allergic encephalomyelitis lesions. The investigator attributes the transfers to the use of recipients which have acquired immunological tolerance to donor lymph node cells, as a result of the spleen cell pretreatment, and in which, therefore, the donor cells can survive and function longer after transfer.

The successful transfer of allergic encephalomyelitis from diseased to healthy animals by means of lymph node cells alone establishes the role of these cells in the development of this disease and the importance of delayed sensitivity in its pathogenesis. These experimental results may furnish the means for answering several important questions about the true nature of allergic reactions to tissue antigens.

Artificially ionized air of no value in therapy of asthma in hospital test

Study of the therapeutic potentialities of artificially ionized air has been underway since before World War II. A report in 1946 of beneficial effects of airborne negative ions on paranasal sinusitis and vasomotor rhinitis prompted inquiry by other investigators into the influence of ionization in hay fever. Prompt amelioration of symptoms appeared to be the outcome.

Withese results in view, Dr. Bernard Zylberberg, of the department of Allergy, National Jewish Hospital, Denver, choose 16 chronically asthmatic men and women, aged 15 to 53, to undergo two 120-minute exposures to ionized air. This collaborative study with Dr. M. H. Loveless, grantee from Cornell University receiving support of the National Institute of Allergy and Infectious Diseases, is described in the Journal of Allergy. With one exception, the patients chosen had remained asymptomatic for at least 3 hours before the test, despite the prohibition of all medication for 12 hours or more prior to the test.

A total of forty 2-hour test periods were evaluated. In 28 instances the patients started the exposure period without symptoms. This clinical pattern was unchanged by exposure to either positive or negative ions. In seven other tests slight or moderate wheezing was already present just before exposure, and symptoms continued unaltered throughout the 120-minute period, regardless of the charge of the ion.

In 5 of the 40 tests, 3 negative, 2 positive, it appeared that mild or moderate wheezing and dyspnea occurred where none had existed prior to the experiment. The authors assume that this might have been the case had no treatment been given, since the ionization had had no demonstrable effect on the symptom-free patients.

The investigators believe that the design of the experiment, essentially double-blind, made it unlikely that results were influenced by psychogenic factors. Their clear-cut findings incline them to discard ionization as therapy for patients with asthma.

Genetically determined factors may play role in sarcoidosis

A complex hereditary factor may be operative in the pathogenesis of sarcoidosis, according to Drs. Richard K. Merchant and John P. Utz of the National Institute of Allergy and Infectious Diseases, reporting in the Archives of Internal Medicine. While much has been learned about this disease during the half century since its initial description, its etiology and pathogenesis have remained obscure. The significance of genetic factors is suggested from the authors' observations of the disease in a mother and daughter, together with reports in the literature of 73 other cases of sarcoidosis diagnosed in more than one member of 32 families.

In support of their postulate, the authors contend that the occurrence of sarcoidosis in parent and offspring, as in the present example, might naturally be expected in a few cases. Furthermore, although the total number of instances of this disease in more than one member of the same family is small (nontwin siblings, 21; identical twins, 6; and parent-offspring, 6) examples in identical twins appear with unexpected frequency. If chance alone determined the development of sarcoidosis in the six pairs of identical twins reported, one would expect twice this number in nonidentical twins. Yet no such reports have been found in the literature. One might also expect many more cases than have been described among nontwin siblings. However, ideal diagnostic criteria have not been fulfilled in many instances in the reported cases of sarcoidosis in more than one member of a family. Moreover, the occurrence of the disease in identical twins is more apt to be reported than its occurrence in other members of a family.

It is concluded that while these findings do not minimize the importance of recent epidemiological and laboratory studies, they do suggest that genetically determined individual consitutional factors may play a role in determining the type or frequency of response that results from exposure to some environmental factor.

PARASITIC DISEASES

Monkey malaria transmitted to humans by bite of mosquito

Transmission of monkey malaria to man through the bite of an infected mosquito—an experimental feat which may compel scientists to reexamine long-established knowledge on the transmission cycle of this disease—has been reported by the Laboratory of Parasite Chemotherapy, National Institute of Allergy and Infectious Diseases.

This finding directly challenges the concept of malaria investigators throughout the world that types of malaria which infect aninals cannot be transmitted to man by the bite of an infected mosquito. Only in the laboratory has it been possible, up until now, to infect man with monkey malaria, and then only by an artificial method: blood inoculation.

Results of the study are summarized in Science, official publication of the American Association for the Advancement of Science. The authors are Dr. Don E. Eyles, Dr G. Robert Coatney, and Dr. Morton E. Getz, all of the Laboratory of Parasite Chemotherapy.

The authors emphasize that the implications of their findings, suggesting the possibility that there may exist in nature a monkey-mosquito-man cycle of malaria infection, remain matters of conjecture at this time. They also point out that no one can say as yet whether this new knowledge will have any practical effect on the course of malaria eradication in areas of the world where monkeys and other nonhuman primates are found.

Referring to these considerations, the authors summarize their views as follows: "We believe that research on lower monkey malarias, with particular regard to the possible existence of reservoirs of human infection, or sources of reinfection of man with new strains, is necessary as an essential adjunct to the present malaria eradication program. We expect to study monkey-human malarias in detail and reexamine the entire question of the host-specificity of primate malarias."

The study reported here originated from accidental infections involving Dr. Eyles and an assistant at the Institute's Memphis Laboratory. In the course of a routine study in which large-scale inoculations of monkeys with primate malaria were being carried out, the two investigators developed illness with fever. Malaria parasites were demonstrated in the blood of both. "Presumably," the authors state, "the source of the malaria was mosquitoes infected with monkey malaria, as neither individual had had any recent contact with human malarias."

Blood taken from each of the infected individuals was injected into uninfected Rhesus monkeys. Both animals developed typical infections 8–10 days later Then, blood from one of the infected workers was then injected into two inmate volunteers at the Federal penitentiary in Atlanta. Both developed clinical attacks of malaria but neither exhibited high parasite densities. These infections are still under study.

The two accidental infections at the Memphis Laboratory were followed by two planned and purposeful infections involving staff members. The first volunteer allowed 30 to 50 *Anopheles freeborni* mosquitoes heavily infected with monkey malaria to feed on him. Eleven and 12 days later he experienced typical symptoms of malaria infection: headache, malaise, and elevated temperature. When parasites could not be demonstrated, a sample of his blood was injected into an uninfected monkey. Six days later the animal came down with malaria, indicating a low-grade infection of the human subject whose blood had been injected into the monkey.

The second staff member allowed himself to be bitten by 10 mosquitoes heavily infected with the strain of primate malaria under study. Fourteen days later he came down with clinical malaria, and parasites were easily demonstrated in his blood. Both volunteers then received standard antimalarial treatment, followed by uneventful recovery.

The parasite causing this disease is known as *Plasmodium cynomologi*, subspecies *bastianelli*, and was recently described by Prof. P. C. C. Garnham of the London School of Hygiene and Tropical Medicine. The new subspecies was isolated from a Kra monkey from Malaya and infected blood was forwarded to the NIH investigators by Professor Garnham for study purposes.

According to the authors, the findings of this investigation underline the need for immediate and intensive studies of monkey malaria in various parts of the world in order to determine their significance.

Fluorescent antibody technic used to demonstrate parasite of human malaria

A diagnostic test which may make it possible for a single laboratory worker to screen many more suspects for malaria in a single day was described at the Ninth Annual Meeting of the American Society of Tropical Medicine and Hygiene, November 2–5, by Drs. John E. Tobie of the National Institute of Allergy and Infectious Diseases Laboratory of Immunology and G. Robert Coatney of the Laboratory of Parasite Chemotherapy.

The new test, based on the fluorescent antibody technique, represents the first recorded instance in which a malaria parasite (*Plasmodium vivax*) has been viewed by this method. As in other tests of this nature, antibodies—in this instance from a serum fraction of a patient harboring the vivax type of malaria—are labeled with a special fluorescent dye (fluorescein isothiocyanate) and the fluorescent antibodies applied to a blood smear containing the malaria parasites. The fluorescent antibody reacts with the parasite, which serves as antigen, so that when the parasites are stimulated with ultraviolet light, they glow. Prior removal of hemoglobin from the blood smear provides a slide in which the red blood cells are not visible—essentially just the glowing malaria parasites.

To evaluate the new procedure, the scientists tested blood smears from seven inmate volunteers known to harbor the vivax type of malaria parasite. Under the fluorescence microscope, each specimen of the prepared parasite—glowing a bright yellow color—stood out clearly from the rest of the field. Using the same procedure, the investigators were able to visualize the parasite of monkey malaria (*Plasmodium cynomolgi bastianellii*) with the same clarity of detail.

Serological tests, such as complement fixation, precipitin or agglutination tests for the diagnosis of malaria, essentially have been of no practical value. For such diagnosis, it has been necessary that well-trained technicians spend many hours in the examination of conventionally stained blood smears. With the new procedure, a far more rapid method of screening is within the realm of possibility. The picture presented under the fluorescence microscope is such that it may be possible for a photoelectric cell to detect the glowing parasites. For this reason, the scientists are currently exploring the possibility of feeding slides of individual test specimens serially through an electronically controlled automatic scanning microscope for the detection of parasites in large-scale surveys.

The scientists emphasized that their studies were strictly of a preliminary nature and that many technical difficulties must be solved before their goals may be achieved.

As a part of their study, the investigators studied the serological relationships between a human malaria parasite, *P. vivax* and a rodent malaria parasite, *P. berghei*. When viewed under the fluorescence microscope, the former glowed approximately three times as bright as the latter, suggesting a distinct difference between the two species. However, when the human type (*P. vivax*) was compared with the parasite of monkey malaria (*P. cynomolgi bastianellii*) both species glowed at essentially the same intensity indicating that they may be closely related malaria parasites.

Despite the relative success of the World Health Organization program to eradicate malaria, nearly half of the world's population continues to live in areas of exposure. Coming at the present time, the new procedure assumes an added significance in view of the further diagnostic difficulties, now being imposed on the already overburdened technician, with the recent discovery that monkey malaria may provide a permanent reservoir for the disease.

Fluorescence of filarial worm suggests new tool in diagnosis of parasitic diseases

The discovery by two National Institute of Allergy and Infectious Diseases scientists that filarial worms may be visualized by a simple fluorescent method in a patient receiving tetracycline offers new diagnostic and therapeutic possibilities in the campaign against parasitic diseases. Dr. John Tobie, Acting Chief of the Laboratory of Immunology, and coinvestigator Dr. Henry K. Beye of the Laboratory of Clinical Investigation have published a detailed description of the work leading to this finding in the proceedings of the Society for Experimental Biology and Medicine.

Investigation of the phenomena was based on the knowledge that tetracyclines fluoresce a yellow-gold color when exposed to ultraviolet light, and on their recent study showing that this series of antibiotics is deposited in filarial worms in vitro. The patient under study was a 15-year old female with so-called fugitive swellings on both trunk and extremities. Examination of a blood sample confirmed the presence of unsheathed microfilariae of *Acanthocheilonema perstans*.

Twenty-four hours after an initial dose of tetracycline (given 1 g. daily by mouth), the patient was placed in a dark room and her skin fluoresced with an ultraviolet hand lamp. Linear, yellow-fluorescent streaks were seen over many parts of the body. When traced at intervals over a 6-hour period, these appeared to migrate in a circular fashion over a 5- to 6-inch area. from these observations, it seemed evident that the worms had selectively taken up a considerably larger amount of drug than the surrounding tissues, which presented only the usual blue-gray autofluorescence of uninvolved skin areas.

According to the scientists, the selective concentration of tetracyclines by microfilariae and adult worms in host tissues may provide two therapeutic possibilities. For one, these antibiotics may themselves have some antifilarial effect, since the treated microfilariae survived less well under ultraviolet stimulation than did the untreated specimens. Second, it may be possible to combine some active antifilarial compound with tetracycline to permit a greater and more rapid concentration of antifilarial drug in worms within the host tissues. Since the tetracyclines can be localized and visualized in worms by fluorescent methods, this might serve as an effective tool in studying the mode of action of these drugs.

Treatment of schistosomiasis with drug stibophen greatly improved by better diet

A series of nutritional studies on mice may have broad implications in the treatment of human schistosomiasis. According to Drs. George Luttermoser and William B. DeWitt of the National Institute of Allergy and Infectious Diseases Laboratory of Parasite Chemotherapy and Laboratory of Parasitic Diseases, the efficacy of stibophen, a common drug used in treating this disease, is greatly improved when the mice are fed an enriched, purified semisynthetic diet. The scientists reported their findings at the Ninth Annual Meeting of the American Society of Tropical Medicine and Hygiene.

When the investigators maintained the mice on a "completely" purified diet, the therapeutic value of stibophen given concurrently was raised to a high degree of effectiveness; when the animals were fed a regular commercial pellet, the drug remained relatively ineffective. In one trial the average worm reduction on the semisynthetic diet was 95 percent, as compared with 12 percent in those mice on a regular commercial laboratory diet. The efficacy of stibophen remained high even when the semisynthetic diet was made low in protein and other chemical factors such as choline, inositol and vitamin B_{12}. This eliminated the general nutritional status of the animals as a cause of the increased therapeutic value of stibophen and implicated specific factors in the diet.

The treatment of schistosomiasis has been unsatisfactory in spite of the many years spent in searching for better drugs. If the results of recent experimental work done with infected animals may be transferred to the human form of schistosomiasis, improved therapy for its victims may be anticipated.

Small amount of chemical effectively controls snail vector of schistosomiasis

In many areas of the world the cost of eradicating schistosomiasis in the usual manner is not economically feasible because of the comparatively large quantity of chemical needed for destruction of the snail vector. However, a series of laboratory experiments by scientists of the National Institute of Allergy and Infectious Diseases indicates that very low concentrations of sodium pentachlorophenate (NaPCP) will drastically diminish the fecundity of the snail, *Austra-*

lorbis glabratus, and result in lowered viability of the eggs produced. Results of the investigation by Drs. Louis Olivier and Willard T. Haskins of the Laboratory of Parasitic Diseases were published in the American Journal of Tropical Medicine and Hygiene.

Experiments were conducted using NaPCP concentrations of 0.05 and 0.1 p.p.m. (parts per million). Although this contrasts with the 10 p.p.m. usually employed in running water and the customary 5 p.p.m. in still water, striking effects on both fecundity and egg viability were observed.

According to the investigating scientists, the effect was especially impressive when the double action of the chemical, i.e., reduction of snail fecundity thus the weakening of egg viability, was considered additively. For example, in one of the experiments, the recovery of viable eggs on the day the test period started was found to be 14.5 e.s.d. (eggs per snail per day). During the subsequent test period the recovery of viable eggs varied from 0.12 to 0.78 e.s.d. In another test, 0.1 p.p.m. of the chemical reduced the production of viable eggs from 11.9 e.s.d. before the addition of chemical to from 0 to 1.03 e.s.d. during the test period.

When destruction of the adult snails by 0.1 p.p.m. of the chemical is considered along with the other action, the overall effect becomes even more striking. Indeed, the viable egg recovery was reduced to 0.11 and 0.81 egg per original snail in the above tests. These are, respectively, 132- and 15-fold reductions from the pretest levels.

All previous field experiments with NaPCP have been designed primarily to kill the adult snails, and the measure of the chemical's efficacy has usually been in terms of adult snail mortality after a short-term treatment with the chemical. The scientists conclude, however, that interference with the reproductive capacity of the snails by the use of very low concentrations of the chemical, even if the adult snails are not destroyed, might reduce or interrupt transmission of schistosomiasis at relatively low cost.

Mosquito control and mass chemotherapy extremely effective against filariasis

An evaluation of the filariasis control program in Tahiti, based on surveys made before and after 5 years of standardized treatment and mosquito control, shows that marked improvement in the control of the disease has been effected during the period under study. The findings are reported by Drs. H. N. March, Jacques Laigret, John F. Kessel, and Ben Bambridge of the Institut de Recherche Medicales de la Polynesie Francaise and the Department of Infectious Diseases, School of Medicine, University of California, Los Angeles, in the American Journal of Tropical Medicine and Hygiene. This work received support from a grant of the National Institute of Allergy and Infectious Diseases.

The surveys were made on a variety of the manifestations of filariasis in the male population of Tahiti. Surveys for both microfilaremia and elephantiasis encompassed all the males of 15 districts, 3,390 in 1949 and 4,262 in 1959 for microfilaremia; also in 1959, 7,360 persons were examined for elephantiasis.

In 1949, 38 percent of the study population demonstrated a positive microfilaremia and 7 percent were affected with elephantiasis. Ten years later the comparable percentages were 6.5 and 2.3. The control program responsible for this sharp decrease consisted of mass treatment with diethycarbamazine, plus elimination of mosquito breeding areas within 100 meters of dwellings.

Diethylcarbamazine (Notezine) was administered in 12 monthly doses of 6 milligrams per kilogram of body weight, with additional treatment to the few with recurrent positive blood films. Drug therapy was well accepted. Persons experiencing lymphangitis attacks often requested medication because they were able to observe at first-hand the benefits of therapy.

No new cases of elephantiasis or hydrocele developed following application of control measures. Another important finding was a drop in cases of elephantiasis from 6.9 percent to 2.2 percent for all males. In the significant laboring-age group (20 to 40), there was a reduction from 5 to 0.6 percent. Total hydroceles were reduced from 9.8 to 3.2 percent. Among males older than 20, acute filarial lymphangitis attacks fell from 36 to 4 percent. In untreated cases, these attacks occur several times a year, often requiring 3 days of bedrest per episode.

Projecting the survey findings to a total rural Tahitian population of approximately 20,000, at least some 500 fewer persons were handicapped by elephantiasis in 1959 than in 1949. In persons over 20, attacks of lymphangitis were reduced from 3,430 in 1949 to 380 in 1959. Conversely, the percentage of that group free from signs of clinical filariasis increased to 49 percent in 1959 as contrasted to 16 percent in 1949. Since no new cases have appeared it is expected that when those now infected die, elephantiasis will cease to exist in those islands where an adequate control program is followed.

Epidemiological survey of State Department employees reveals new facts on amebiasis

Results of a survey of State Department employees reveal a surprising lack of correlation between infection with Entameba histolytica and job absenteeism, weight loss or excessive report of diarrhea and abdominal pains.

The survey was carried out jointly by Drs. Donald E. Kayhoe, Henry K. Beye, and Elizabeth Guinn of the National Institute of Allergy and Infectious Diseases Laboratory of Clinical Investigation; and Dr. George P. George of the State Department. It involved nearly 6,000 of the more than 35,000 employees and dependents stationed outside the United States. The scientists reported their findings at the Ninth Annual Meeting of the American Society of Tropical Medicine and Hygiene.

Most of these individuals relied on local facilities for food, water, sanitation, and medical care. Frequently their meals were prepared according to the prevailing culinary and sanitary customs. Sixteen percent reported no running drinking water in their place of residence and almost all utilized local household servants.

Each participant submitted a stool specimen which was forwarded to the National Institutes of Health for study. Laboratory findings were correlated with replies to questionnaires to provide a rough measurement of the effects of intestinal parasitism on the health of these individuals during their assignment overseas.

Answers to one of the questionnaires on health status were compared against individuals free of parasites, and those harboring *Entameba histolytica* or *Giardia lamblia.* While more of those with *E. histolytica* believed their health was poorer than usual, little difference was found between the three groups in respect to time lost from work. Diarrhea was commonplace, yet, surprisingly, the sufferers included almost as many harboring the ameba as without. At one time, the presence of the parasite was always assumed to be synonymous with overt symptoms of disease. This is now known to be false.

Atabrine employed as new treatment of beef tapeworm infestation

A more effective treatment for beef tapeworm infestation may result from the use of atabrine administered through a duodenal tube according to Drs. Donald E. Kayhoe and Henry K. Beye of the Laboratory of Clinical Investigation. The scientists reported their findings at the Ninth Annual Meeting of the American Society of Tropical Medicine and Hygiene.

The study group consisted of 23 patients including 15 who had been unsuccessfully treated by conventional methods. A concentrated solution of antabrine was administered directly into each patient's duodenum with a Rheyfus tube whose position had first been verified by X-ray.

Thirty minutes later the patients were purged with sodium sulfate solution via the tube and stools were examined for the head of the tapeworm. Those who did not pass the entire parasite at this time were followed for at least 1 year and, if stools remained negative, they were presumed cured. The regime was successful in 20 of 23 patients studied.

New diagnostic test for bovine leptospirosis superior to older methods

At the present time, leptospiruria may be demonstrated by direct darkfield examination, cultural procedures or laboratory animal inoculations. The darkfield method is limited in requiring the presence of a relatively large number of organisms. Use of cultural procedures requires aseptic collection of urine. Inoculation is time-consuming and expensive because the animals must be maintained over a period of time before results are known. A report in the Journal of Immunology describes a modified urine hemolytic test for diagnosing bovine leptospirosis without some of these limitations. The author of the report, Dr. Leif M. Ringen of Washington University, St. Louis, is a grantee of the National Institute of Allergy and Infectious Diseases.

The procedure described by the scientist is a modification of the hemolytic test reported by Dr. Cox in 1955 for the serodiagnosis of leptospirosis using *Leptospira biflexa* as the source of the erythrocyte sensitizing substance. In Dr. Cox's test, a genus specific reaction is obtained when complement and the sensitized sheep red blood cells are incubated in the presence of specific antibodies. Dr. Ringen's modification uses a soluble erythrocyte sensitizing substance which is precipitated out of bovine urine during the leptospiruria period.

For comparative purposes, the scientist infected a group of calves experimentally with *Leptospira pomona.* Urine was collected from these animals at weekly intervals and inspected for the presence of leptospires by direct darkfield examination, inoculation into laboratory animals and by the new procedure. The scientist found that leptospiruria may be demonstrated by animal inoculation before the urine hemolytic reaction becomes positive, or vice versa. However, in the latter stages of the disease, the urine hemolytic test continued to be positive after leptospiruria could no longer be demonstrated by animal inoculation. In one group of 116 urine samples, 14 percent were positive and 36 percent negative by both procedures, 42 percent positive to the modified test alone, but only 8 percent positive to animal inoculation alone. In other animals tested, leptospiruria could be demonstrated only by the modified test. It was difficult to determine the actual numbers of leptospires that could be detected by this procedure, but positive results were obtained from infected urine diluted as much as 10,000 times.

Intestinal parasitism continues in hospital despite improvement in environment

The high incidence of intestinal parasitism in patients in mental institutions has been attributed variously to crowded conditions and to inherent untidiness among these patients. A unique study designed to determine the possible relationship between housing facilities and parasitism in mental patients reveals that transmission of intestinal protozoa continued despite greatly improved housing and sanitation of the group during the 3 years of the study.

Dr. Geoffrey M. Jeffery of the National Institute of Allergy and Infectious Diseases Laboratory of Parasite Chemotherapy field station in Columbia, S.C., reports his findings in the American Journal of Hygiene. Prior to removal to modern quarters from an extremely outmoded building, a core group of 110 white female patients ranging in age from 18 to 76 years were examined for intestinal parasites. Nine series of examinations were conducted, four during the first year (1954), three the second, and two the third year. This group was studied for the entire 3-year period and was examined on all nine occasions. In addition, 199 patients had 1 to 8 examinations, depending on the length of time they remained at the South Carolina State Hospital, site of the study.

The physical environment of the patients was also checked regularly, including gross inspection for fecal contamination of the buildings and exercise yards, plus surface sampling of floors, walls, and furnishings by the use of cellulose tape. Twenty-six sites within the building were samples for examination each time.

The incidence of seven protozoan species from infected inmates was tabulated. Of these species (*E. histolytica, E. coli, I. butschlii, E. nana, C. mesnili, T. hominis,* and *G. lamblia*) only *C. mesnili* and *T. hominis* showed a net decrease in incidence between initial and final examinations. Some helminths (hookworm, Strongyloides, Trichuris) were also surveyed, and a small reduction in the percentage of patients infected was observed; of these, *Strongyloides stercoralis* showed the most pronounced reduction.

A single striking increase in incidence was observed in the protozoon *E. nana.* With this organism, an initial 19.1 percent incidence rose to 62.7 percent on final examination.

Dr. Jeffery believes his data justify the assumption that transmission of protozoa continued steadily throughout the study. The rate of acquisition of protozoa appeared to lessen, however, during the last year or more of residence in the new quarters. The helminths present a different picture. After the patients were transferred to a modern building, there was no evidence of hookworm transmission, and only three cases of *T. trichiura* occurred which could be attributed to residence in the new building.

The question of persistence of parasitic protozoa, according to Dr. Jeffery, is clouded by the distinct possibility that prolonged occurrence of a given parasite in an individual might represent a number of infections of short duration rather than a signle prolonged infection. In extrapolating probable percentages of infections within periods of 5, 10, and 20 years, based on average percent of infection per year, in general the parasite species which apparently persist for the longest periods are those with the highest prevalence at any one time. The persistence of hookworm and *T. trichiura* infections for the full 3-year period in almost all cases is indicative of the normally long persistence of these parasites in untreated populations. In work subsequent to that described in this report, it has been shown in this same group that these parasites continue to persist in the majority of cases for a total of at least 5 years.

Indirect hemagglutination effectively detects parotistic disease clonorchiasis

The successful demonstration that infection with *Clonorchis sinensis* can be detected by the indirect tanned-cell hemagglutination (IHA) test adds a new diagnostic tool against clonorchiasis, a liver fluke disease highly endemic in the Far East. This work is reported in the American Journal of Tropical Medicine and Hygiene by investigators Guillermo Pancheco, Dale E. Wykoff, and Rodney C. Jung of Tulane University School of Medicine, whose study was supported by a grant from the National Institute of Allergy and Infectious Diseases.

C. sinensis occurs as a common parasite of fish-eating mammals. It causes human infection in Japan, Korea, and China. The human disease has also been recorded in Chinese inhabitants of the United States, Cuba, and India, and in native Hawaiians. Man acquires the infection by eating raw, inadequately cooked. fresh-water fish. Dried, salted, or pickled flesh of infected fresh-water fish is also a source of the disease in man.

Clonorchiasis responds to treatment with oral gentian violet. Given in the early stages, this medication is believed curative, and may be beneficial even in advanced cases.

Four different sources of sera were used in this study: (1) rabbits experimentally inoculated with metacercariae of *C. sinensis;* (2) human beings infected with the organism; (3) humans infected with a variety of other parasites; and (4) animals experimentally or naturally infected with other parasites.

The IHA test proved sensitive in detecting *C. sinensis.* Compared to the complement fixation test previously used, less extract (4 percent) produced a titer 40 times greater in the IHA test. This result is in agreement, say the authors, with trials of similar tests for *Echinococcus.* Other investigators have used indirect hemagglutination on a variety of parasites, including *Schistosoma, Trichinella, Echinococcus* and ascarids, with equal effect.

Specificity as well as sensitivity of the IHA test was found to be increased by treating the test material with ether prior to saline extraction.

The relationship between the antigen-antibody systems demonstrated by IHA and by CF has not been determined. The antibody titers found by IHA in experimental infections in rabbits appear to rise early in the infection, reaching a peak between the 6th and 16th weeks and then decreasing. A similar rise and fall of antibody titers has been reported by other investigators who used a CF test.

BACTERIAL DISEASES

New synthetic penicillin proves promising against severe bacterial infections

A synthetic penicillin (X–1497) which may be effective against certain forms of resistant staphylococcus has been tested by scientists of the National Institute of Allergy and Infectious Diseases with promising results.

The new drug was first developed commercially by Beecham Laboratories in England. Under the trade name, staphcillin, the U.S. Bristol Laboratories, which has an arrangement with Beecham, released it to the National Institutes of Health and others for clinical and biochemical tests. Results were presented at a symposium sponsored by the State University of New York, Upstate Medical Center, at Syracuse, to bring together available knowledge concerning the new drug.

In discussing its biochemical aspects, Dr. Harry Steinman of the Laboratory of Clinical Investigation observed that the new synthetic, in contrast to penicillin G (the form of the drug commonly employed against infection) was almost completely resistant to destruction by penicillinase (a staphylococcal enzyme whose production is stimulated in the presence of penicillin). Yet, paradoxically, staphcillin is 10 time as active in inducing penicillinase production in resistant staphylococcus.

In the clinical trials, Drs. David Rifkind and Vernon Knight of the same laboratory administered the drug to 10 patients with a variety of severe staphylococcal and streptococcal infections. Typical among these patients was a 27-year-old housewife who had been treated for staphylococcal bloodstream infection with tetracycline, penicillin G, chloramphenicol and erythromycin, without success. Twenty-one days of therapy with penicillin X-1497 resulted in an uneventful and sustained recovery.

Another patient, a 9-year-old male, had suffered recurrent staphylococcal infections for most of his lifetime. These included, among others, 10 episodes of penumonia, 4 of bloodstream infection and innumerable abscesses. Thirty-five days of therapy resulted in the disappearance of fever and healing of all skin lesions. Cultures derived from the nose and liver no longer harbored the organism. As with the above, all other cases of infection were followed by recovery or other evidence of effective antimicrobial activity after treatment.

The scientists commented that the present difficulties in the treatment of severe staphylococcal infections are derived largely from the fact that many cultures are resistant to the older penicillins, making even huge doses of drugs ineffective. Moreover, infections in which large populations of staphylococci are present, even though susceptible, may respond poorly to treatment with these drugs. In contrast, penicillin X-1497 has thus far proven active against all strains of staphylococci tested, even those that are resistant to the older penicillins. And finally, the new penicillin has been found to be active against large populations of staphylococci.

In a separate study conducted by Dr. Richard Aster of the National Institute of Arthritis and Metabolic Diseases, results suggest an immunological difference between penicillin X-1497 and other penicillins and indicate the possibility that the new drug may be tolerated by those individuals allergic to penicillin G. The investigator tested serum specimens from one of the cases for antibodies against penicillin X-1497. Although antibodies were noted for other penicillins, presumably from previous treatment, none was found in response to the new synthetic drug.

New variable of staphylococcus epidemics in hospitals is concomitant virus infection

"Cloud babies," infants who showed no overt sign of disease but assumed highly infectious roles in hospital nursery staphylococcus epidemics, are described for the first time in a study supported by the National Institute of Allergy and Infectious Diseases. Respiratory viruses, which operate independently of staphylococcus, appeared responsible for the high infectiousness of the "cloud baby" in a number of nursery epidemics reported by Dr. Heinz F. Eichenwald and associates in the American Journal of Diseases of Children.

The authors point out that although neonatal staphylococcus is a substantial cause of death in infancy and consequently has received much attention throughout the world, the complexity of modern medical institutions has made it a difficult disease to study. However, their detailed studies on the spread of staphylococci in a number of different nurseries at the New York Hospital-Cornell Medical Center showed that newborn infants infected with staphylococci may fall into one of two distinct groups.

The majority of babies examined possessed a low index of infectivity, while a small minority were highly infectious. Because infants of the latter group were literally surrounded by clouds of bacteria, they are designated "cloud babies" in the report. Followup studies showed that their explosive role in the hospital epidemics continued, after discharge, within the family unit.

The bacteriologic factors that determine whether any given infant becomes a "cloud baby" were investigated by use of air-samplers and epidemiologic techniques. The clinically well "cloud baby" contaminated the atmosphere chiefly from the respiratory tract, with skin, cord, or clothing representing only a minor source of microbes.

The investigations also showed that a factor is responsible for the "phenomenon of cloudiness" which operates independently of the staphylococcus, is itself infectious, and has a distinct epidemiology of its own. This factor appeared to consist of a number of respiratory viruses occasionally encountered in hospitalized newborn infants. Adenovirus type 2 and ECHO virus type 20 were isolated from two of three test groups.

During the observations it was possible to compare the degree of infectivity of nondisseminating staphylococcal carrier babies and "cloud babies." Two carrier babies were transferred into a nursery that had been under close observation for several weeks and in which the number and identity ot infected infants and staff were known. During a 4-day stay by the carrier babies and for 4 days thereafter no contamination of the nursery air could be demonstrated, the staff continued to have negative cultures, and only 1 of 41 infants in the nursery became infected with *Staphylococcus aureus* type 80/81.

Following this determination, another baby was transferred into the unit. He was removed after a 2-day stay when it was discovered that he was a "cloud baby"; nevertheless, colonization rates among the infants increased within 24 hours after his arrival. Within a few days about one-half of the babies had been converted to carriers of *S. aureus* type 80/81. Five days after his departure, other "cloud babies" were found in the unit. The presence of these new "cloud babies" was paralleled by a rise in the number of staphylococci type 80/81 in the air of the nursery and by the appearance of nasal carriers of the organism among the staff. This comparison was again demonstrated in a subsequent controlled situation set up by the scientists.

The report does not minimize the importance of the adult carrier as a source of infection. Though the exact condition under which adult carriers infect infants is unknown and the transmission route has not been clearly established, obviously both staphylococci and viruses must be acquired from someone. It is probable that in ventilated nurseries of adequate size, designed for four or five babies, hospital personnel are of obvious significance, while under conditions of overcrowding, the "cloud baby" may assume a greater relative importance in the genesis of epidemics.

The explosiveness of the "cloud baby" outbreaks, the authors say, forces consideration of airborne dissemination in the design of nursery units. Forced ventilation with frequent air changes, as well as the reinvestigation of ultraviolet light as an additional method of air sterilization seems to the authors the greatest protection against airborne spread.

The authors also note that all carriers of *S. aureus* type 80/81 in the study continued to harbor the organism despite novobiocin therapy, whereas those babies who received the antibiotic prior to infection were almost uniformly protected.

Early detection and treatment of asymptomatic bacteriuria averts urinary tract infection

Development of a reliable test for the detection of early cases of pyelonephritis was prompted by the finding at autopsy of a 10 to 20 percent incidence of that disease, which is often unsuspected or misdiagnosed. Dr. Edward H. Kass of Harvard University described at the Chicago Medical Society annual clinical conference a study of the relationship of bacteriuria to serious kidney disease. Dr. Kass has also published his findings in the A.M.A. Archives of Internal Medicine. This work received grant support from the National Institute of Allergy and Infectious Diseases.

To perform the simple test, urine specimens are collected under reasonably antiseptic conditions. Bacterial colony counts on the fresh specimens are then made. Counts greater than 100,000 per milliliter generally indicate the presence of true bacteriuria, which is actual multiplication of bacteria within the urinary tract. Two separate counts are made before the test is considered diagnostic. Three-fourths of infected patients respond to treatment with sulfonamides (0.5 gram daily for 1 or 2 weeks). Alternative therapy on the basis of sensitivity studies is used for patients resistant to sulfonamides.

Dr. Kass has observed that pyelonephritis of pregnancy occurs almost exclusively in patients who have bacteriuria at the time of the first prenatal visit. The way is now clear, with this test, for the virtual elimination of pyelonephritis among pregnant women.

In a group of 90 pregnant women at Boston City Hospital, patients with asymptomatic bacteriuria who were less than 8 months' pregnant were divided into two groups on an alternating basis. One group received a lactose placebo, the other was treated until term. Incidence of pyelonephritis in the control group was 42 percent. There was no symptomatic infection in patients whose bacteriuria had been eliminated by treatment.

Followup data have been obtained 3 to 12 months post partum. Incomplete results to date indicate that about three-fourths of the untreated patients were still infected 3 months after delivery but more than three-fourths of the treated patients were free of bacteriuria when studied 3 to 12 months post partum.

Based on the observation that 30 percent of female and 10 percent of male patients have pyelonephritis, Dr. Kass suggests that every medical patient be considered a potential candidate for this disease. It occurs widely not only in pregnant women but in persons suffering from obstructive diseases of the urinary tract, diabetes mellitus, hypertension and uremia, and is also one of the commonest causes of acute renal failure.

Penicillin reduces mortality in experimental staphylococcosis under test conditions

Results of a study reported by grantees of the National Institute of Allergy and Infectious Diseases may help to define the disputed value of penicillin against infections caused by penicillin-resistant staphylococcus. Drs. Donald B. Louria and David E. Rogers conclude, in a report in the Journal of Laboratory and Clinical Medicine, that penicillin can under certain circumstances significantly reduce the mortality resulting from infection produced by injecting large numbers of penicillin-resistant staphylococci into mice. The most important circumstances affecting the outcome of treatment are the amount of penicillin employed and the time therapy is begun.

In a series of experiments employing a highly virulent strain of staphylococcus, the scientists found that the total mortality in untreated mice ranged from 80 to 100 percent, with only 4 of 117 mice surviving the experimental period. When penicillin treatment was started within 4 hours after infection, survival was prolonged and rates of mortality reduced. For example, in mice receiving 4,000 to 10,000 units of penicillin daily, although death was delayed, at least 75 percent of the mice in each group eventually died. When 40,000 units of procaine penicillin or 100,000 units of aqueous penicillin were administered the mortality was reduced to 50 and 25 percent respectively.

Delaying treatment 24 to 48 hours after infection markedly reduced the beneficial effects of penicillin. Survival rates varied from 0 to 25 percent and did not correlate well with the amount of penicillin administered. In animals receiving early treatment, survival rates ranged from 3 to 75 percent and were well correlated with the quantity of penicillin injected. When treatment was begun 4 hours after infection, at least 45 percent of the mice receiving 20,000 units of penicillin twice daily survived. In contrast, prolonged survival was uncommon in animals receiving delayed treatment regardless of the dosage employed, although death was often significantly delayed. Thus, both the dose employed and the time at which therapy was initiated had a significant effect on the outcome of the penicillin-resistant staphylococcal infection.

Neither the time of administration nor the dose of penicillin employed appeared to be of critical importance in the treatment of a similar infection in mice produced with a penicillin-susceptible strain of staphylococci. Virtually all treated animals infected with the penicillin-sensitive strain survived whether treatment was started 4 or 24 hours after infection.

Time-saving new test determines potential pathogenicity of clinical staphylococcus

An observation that potentially pathogenic staphylococci may be differentiated from harmless strains by their ability to reduce tellurite underlies the successful development of a new and reliable test by scientists of the University of Utah College of Medicine and the Clinical Microbiology Laboratory, Salt Lake County General Hospital, Salt Lake City, Utah. Dr. Hoeprich and associates, who published the results of the study in the Journal of Laboratory and Clinical Medicine, are supported by a grant from the National Institute of Allergy and Infectious Diseases. The data presented in the grantees' paper indicate that testing for tellurite reduction provides information of the same significance as testing for coagulase production.

Ability to reduce tellurite is quite simply assayed. Isolates to be tested are streaked on a sector of a tellurite-glycine agar plate; eight tests are conveniently done on one plate. After overnight incubation the plates are inspected for the presence of jet black colonies indicative of growth with reduction of tellurite. With periods of incubation much in excess of 18 hours, some staphylococcal isolates which show no growth, or at most a grayish to brownish smudge in 18 hours, will develop black colonies. Not only is tellurite reduction conveniently carried out, but the cost per test is quite small—about one-half cent per test when eight isolates are inoculated per plate.

Direct evidence presented that penicillinase is inducible enzyme of staphylococcus aureus

Further evidence to support the contested view that penicillinase is an inducible enzyme of *Staphylococcus aureus* was cited at the 1960 meetings of the Federation of American Societies for Experimental Biology, in a paper read by Dr. Harry Steinman of the National Institute of Allergy and Infectious Diseases Laboratory of Clinical Investigation.

In this study Dr. Steinman used an organic mercury derivative to inactivate the bacterium without affecting its penicillinase activity, thus permitting exact analysis of the enzyme. Enzyme activities were demonstrated by testing samples removed from a reaction mixture at periodic intervals. Curves plotted from these data were similar to those obtained by continuous observation of the same reaction system.

The greater accuracy obtained by this method allows more precise evaluation of the experimental curves. Thus the formation of new enzyme was apparent in a synthetic medium within 15 minutes after exposure of the organism to penicillin and the rate of increase was linear with time. This method also permitted studies on variation of the inducing concentration of penicillin, without interference by the high levels of penicillin required in the subsequent assay procedure. In this way it was established that very high concentrations of penicillin were required for this reaction by the particular strain of *S. aureus* examined.

More direct evidence for the induced formation was obtained from studies on cell-free preparations wherein concentrated suspensions of *S. aureus* broken up by bombardment with fine glass beads were found to possess good penicillinase activity.

By means of adsorption and elution of the cell-free enzyme preparation, and fractional precipitation with ammonium sulfate, followed by isoelectric precipitation—a method not hitherto applied to staphylococcal penicillinaise—concentration and partial purification of basal penicillinase from organisms not exposed to penicillin was achieved. The increased activity obtained in cell-free extracts from penicillin treated cultures persisted through the purification procedures, indicating that new, induced protein had been actually formed. However, the preparations were still relatively impure since the specific activities were not identical with each other.

A comparison of the physicochemical properties of partially purified penicillinase from *S. aureus* with purified penicillin from *B. cereus* indicates that the two enzyme proteins are not identical.

Combination of novobiocin and tetracycline fails to demonstrate synergistic action

A controlled study to determine possible synergistic effect on the antibacterial activity of human serum resulting from the combined administration of novobiocin and tetracycline has revealed only additive or indifferent results. Drs. Hans A. Hirsch and Maxwell Finland report this finding in the New England Journal of Medicine. Their study was aided by a grant from the National Institute of Allergy and Infectious Diseases.

The investigators gave eight young men four single doses of the antibiotics at 5-day intervals as follows: 750 mg. of novobiocin; 500 mg. of novobiocin in combination with 250 mg. of tetracycline; and 750 mg. of tetracycline. One week later, all subjects received an additional single capsule of 250 mg. of novobiocin. Blood was taken before breakfast and at 2, 4, 6, 12, and 24 hours later. Serum from each blood was separated and divided into two rubber-stoppered tubes. One set of serum was assayed for antibacterial activity by a two-fold dilution method in broth, using the following four test organisms: staphylococcus 209P, streptococcus 98, staphylococcus 400 and staphylococcus 195.

In general, novobiocin was more rapidly absorbed than tetracycline, but the levels in the serum resulting from the former fell more rapidly. As a result, the levels at 2 hours were highest when novobiocin activity predominated. When tetracycline activity predominated, the average levels were highest at 4 hours and thereafter. This became particularly obvious at 24 hours, the height at that time being in the same order as the amount of tetracycline in the dose.

These relations were best illustrated in the activity against staphylococcus 209P, which was somewhat more sensitive to novobiocin than to tetracycline. Here, the average levels were highest throughout after 750 mg. of novobiocin except at 24 hours, when the highest level resulted from 750 mg. of tetracycline. As the ratio of tetracycline to novobiocin in the dose increased, the average peak levels dropped, and the levels thereafter were increasingly better sustained. The observed differences in the peak levels were all significant except between the doses of 250 mg. of novobiocin with and without 500 mg. of tetracycline. All the differences in total activity resulting from the various doses were also significant except those between the doses of 500 mg. of tetracycline combined with 250 mg. of novobiocin and 750 mg. of tetracycline.

These observations suggest that the combined antibacterial activity resulting from doses of novobiocin in combination with tetracycline was predominantly additive or indifferent. Certainly, no synergistic effect was demonstrated, but a possible antagonistic effect against the tetracycline-resistant staphylococcus 400 resulted in the serum from the administration of 500 mg. of tetracycline together with 250 mg. of novobiocin.

Enhanced susceptibility to bacterial infection after whole body X-ray studied

A series of studies supported jointly by the University of Chicago, the U.S. Atomic Energy Commission and the National Institute of Allergy and Infectious Diseases has clarified important details surrounding the known fact of increased mammalian susceptibility to infection after whole body exposure to moderate doses of radiation. Drs. C. Phillip Miller, Carolyn W. Hammond and Sonia K. Anderle made their investigations at the Argonne Cancer Research Hospital in Chicago and published results in the Journal of Experimental Medicine.

In the experiments the scientists randomly distributed young adult mice into groups of 10 to 20, and exposed them to one of the following doses of X-radiation—300, 400, 500, and 600 r. (roentgen units). The mice were then challenged with a virulent strain of *Pseudomonas aeruginosa.*

In the 400 and 500 r. series susceptibility to infection increased rapidly up to the third day after irradiation. In the former, it declined thereafter; but in the latter it was maintained until the 11th day. Each series had returned to normal by the 20th day.

Exposure to 300 r. caused but slight increase in susceptibility to experimental infection. Exposure to 600 r. was followed by a very marked increase, but caused so many radiation deaths that the results of the inoculations are not comparable with the others.

Mice in the 400 and 500 r. series were injected via 2 routes, intraperitoneally and intravenously (dorsal tail vein). Those challenged by the latter method displayed a higher susceptibility to infection. The difference was found to be due to the regular appearance of a small focus of infection at the site of injection as a result of leakage of inoculum into the surrounding tissues. Bacterial multiplication occurred in these locations in irradiated mice, but not in unirradiated mice, nor at the site of intraperitoneal inoculation even in irradiated mice.

FUNGUS DISEASES

Crystalline hemolytic component of fire ant venom has antifungal effect

A crystalline hemolytic component of fire ant venom inhibited the activity of 15 of 21 organisms, mostly human pathogens, demonstrating antimycotic action by a lack of growth immediately surrounding a crystal of this material placed in direct contact with the fungi tested.

This research, an extension of studies of others which indicated the antibiotic character of fire ant venom, is reported by Drs. James T. Sinski, George A. Adrouny, Vincent J. Derbes and Rodney C. Jung, National Institute of Allergy and Infectious Diseases grantees working at Tulane University School of Medicine in New Orleans. The investigators caution that their report is not to be interpreted as a study on the antimycotic effects of this material for future clinical use but should be considered an attempt to broaden methods for characterizing biologically the crystalline material obtained from fire ant venom.

The tropical fire ant (*Solenopsis saevissima*) introduced into the United States at Mobile, Ala., about 1920 is not only a growing agricultural problem in the Southeastern United States but a menace to human beings. The sting of this insect is extremely painful and can cause severe allergic reactions, including anaphylactic shock.

In the experiments reported in the proceedings of the Society for Experimental Biology and Medicine fungi were streaked onto Petri dishes containing a medium of 2 percent glucose, 1 percent yeast extract, 1 percent casamino acids, and 2 percent agar in distilled water. All cultures were tested with a single lot of crude crystalline venom. A few cultures were were also tested with a recrystallized venom. A small crystal of venom on each seeded plate was incubated at room temperature, and results were recorded when growth was at its maximum. Inhibition of growth immediately surrounding the crystal occurred with the following: Balstomyces, Candida, Cladosporium, Cryptococcus, Geotrichum, Hormodendrum, Microsporum, Nocardia, Phialophora, and Trichophyton.

Emmonsia crescens, new fungus pathogen of rodents, described

When inhaled by its rodent host, a spore of *Emmonsia crescens* is 3 to 4 microns in diameter. The spores grow to a maximum diameter of 480 microns, 1 million-fold increase in volume, which is extremely unusual in the microbiological world. This fungus was described by Dr. C. W. Emmons, head of the Medical Mycology Section of the Laboratory of Infectious Diseases, and Dr. W. L. Jellison, senior parasitologist, Rocky Mountain Laboratory, National Institute of Allergy and Infectious Diseases, during the 2-day second conference on medical mycology of the New York Academy of Sciences.

Having increased 1 million-fold in volume the spores are incapable of further growth and do not reproduce as long as they remain in the animal. In spite of their enormous size, which makes them easy to see with the naked eye, these fungus cells cause little host reaction except physical displacement of pulmonary tissues. After a month, if the cells are removed to a culture tube from the lung, they germinate by sending out dozens of germination tubes. After several months they may die and calcify.

The fungus has been named *E. crescens* to denote the immense increase in the size of the fungus cell. The disease it causes in rodents is called adiaspiromycosis to signify the failure of the fungus to disseminate in the animal. In spite of the size of the fungus and its wide geographic prevalence, pathologists and mammalogists appear either to have overlooked it or perhaps have mistaken it for a worm or other parasite. It has not yet been found in man.

Dr. Jellison, collecting and studying material in Europe during the summer of 1959, found *E. crescens* in Norway, Sweden, Finland, France, Yugoslavia, Africa, and within 50 miles of the Arctic Circle. In Stockholm, examining preserved museum specimens, he found it in a vole trapped 115 years ago. Dr. Jellison has also discovered the fungus in rodents of the United States, Korea, and Ecuador.

In 1942, Dr. Emmons found a similar fungus that was frequent in the lungs of rodents in southern Arizona. This was designated Haplosporangium. Recently it was transferred to a new genus, Emmonsia, by Italian mycologists Ciferri and Montemartini.

Prevalence and adaptability of fungal disease agents delineated

Dr. Chester W. Emmons of the National Institute of Allergy and Infectious Diseases indicated in his presidential address before the Mycological Society of America meeting in Stillwater, Okla., that "mycologists must continue to take increasing responsibility in the study of the fungi" which cause systemic mycoses. In one recent year mycotic deaths in the United States equaled the number of poliomyelitis deaths and exceeded by one the total number of deaths reported for whooping cough, diphtheria, scarlet fever, typhoid, malaria, and brucellosis.

The head of NIAID's Medical Mycology Section pointed out that although mild or fatal systemic mycoses of man are not contagious, their causative agents are present in widespread areas of man's environment. The fungi responsible for systemic mycoses may grow and reproduce indefinitely in soil and humus as saprophytes, yet retain the ability to produce lethal disease in man. They possess characteristics which enable them under proper circumstances to turn immediately from a saprophytic existence to parasitism of animal tissues.

Their adaptability and prevalence, Dr. Emmons noted, indicates that medical mycology does not deal with "a bizarre group of rare fungi but with molds and yeasts with which man may be in daily contact." He also pointed out that the systemic mycoses remain difficult to treat while morbidity and mortality from bacterial disease have been reduced greatly by antibiotic therapy.

Causative agents referred to by Dr. Emmons included *Coccidioides immitis, Nocardia asteroides, Histoplasma capsulatum, Cryptococcus neoformans, Aspergillis fumigatus, Absidia corymbifera* and species of Rhizopus. Any of these can cause fatal mycoses and can be isolated easily and regularly from soil habitats. Other fungi which cause potentially fatal diseases are assumed on good evidence to have saprophytic existence and several fungi which cause chronic but rarely fatal diseases have been isolated from man's environment.

The NIAID mycologist discussed in detail several of the more familiar saprophytes which sometimes play a lethal role, including *Cryptococcus neoformans*, the causative agent to cryptococcosis. *C. neoformans* is readily isolated in pigeon droppings on window ledges of office buildings and beneath roosting sites in open attics of old buildings in cities, as well as in barns and haymows on farms.

"These are virulent strains of the fungus, indistinguishable from those found in fatal cases of cryptococcal meningitis," Dr. Emmons said, stressing that "the public health implications of the common occurrence in man's environment of a fungus capable of causing fatal meningitis need careful evaluation."

Some experimental fungal infections enhanced by cortisone

Experimental Candida infections in mice are enhanced to a far greater degree by cortisone than those due to *Histoplasma capsulatum* or *Cryptococcus neoformans*, according to a report appearing in the Journal of Clinical Investigation. Drs. Donald B. Louria, Nancy Fallon, and Harry G. Browne, authors of the report, received grant support from the National Institute of Allergy and Infectious Diseases.

Although many experimantal infections are known to flourish following steroid administration, there is very little information on the relative disposition of the various species of fungi to disseminate in the presence of coritsone, nor is there any definitive data on the mechanisms involved or on tissue localization.

The investigators found that the administration of large amounts of cortisone produced a marked increase in the mortality of mice infected with Candida but does not enhance infections due to *H. capsulatum* or *C. neoformans* no matter what the quantity of inocula used.

Tissue census studies made by the scientists suggested that in cortisone-treated mice infected with this strain of *C. albicans* the increased mortality was related specifically to increased multiplication of the fungus in the kidney. Although the exact mechanisms underlying renal susceptibility to infection are not yet delineated, detailed histological studies indicated that renal localization of infection in normal and cortisone-treated mice was related to rupture of the fungus into tubular lumina. Once within the tubule the fungus appeared to be protected from host defenses and multiplied unihibitedly. Whereas extensive intra-tubular residence was uncommon in normal mice injected with large quantities of cells, it occurred uniformly in cortisone-treated animals.

On the basis of their investigations, Dr. Louria and his associates concluded that the time of cortisone administration appears to be highly significant in determining the degree to which Candida infection may be amplified. A single day's delay in treatment markedly reduces the effects of the hormone. When cortisone is administered 7 days after infection amplification of infection becomes negligible.

RICKETTSIAL DISEASES

Q fever infection in cattle found to occur in all parts of the United States

Data now available demonstrate conclusively that Q fever occurs among dairy cattle in all parts of the United States. State or local health and agricultural groups in 26 States participated in recent surveys which confirm and expand earlier findings and prove that there is considerable bovine infection in 19 States not previously surveyed. These data are reported by Dr. Laurie Luoto in Public Health Reports. Dr. Luoto is on the staff of the Hamilton, Mont., Rocky Mountain Laboratory of the National Institute of Allergy and Infectious Diseases.

Over 24,000 herds were tested, including dairy cattle along the supposedly infection-free eastern seaboard, where high levels of infection were demonstrated. An unexpectedly high herd infection rate was encountered in most sections of the country, ranging from 1 to 65 percent. A significant spread of infection has been noted among herds in Idaho, Montana, and in other States. The increase of bovine Q fever, even within herds maintained under dispersed rural conditions, suggests its propensity for becoming a greater source of human infection.

Milk specimens and serums were tested for antibody against *Coxiella burnetii,* causative organism of Q fever, using the capillary-tube agglutination test (CAT). This procedure, used in Q fever studies since 1952, has been found to be specific, sensitive, and reproducible. A close correlation exists between the presence of the agent in milk and of agglutinating antibody in milk or serum of individual animals. The test works effectively under field conditions, detecting infection in herds and animals in areas where rates of infection among individual cows are only a fraction of 1 percent.

Not only were herd infections widespread, but a high percentage of infection occurred among animals within herds, ranging above 50 percent within some herds. Even in areas where infections are infrequent, high levels of infection exist within individual herds. For example, in Montana, where only 1 percent of herds are infected, up to 72 percent of cows in herds were positive.

In view of the widespread prevalence of bovine Q fever throughout the United States,[1] Dr. Luoto believes that information on associated human infections is urgently needed. Human infections occur and are diagnosed in areas where Q fever is known to exist in animal reservoirs. Human Q fever is already recognized as a public health problem in some areas. In southern California at least 300 human cases were detected, and 350 cases were associated with sheep in northern California during epidemiological studies in 1948–49.

The true incidence of human infection within this country is unknown because many cases may go unrecognized. Even during an acknowledged epidemic in Idaho during 1958, most of 93 laboratory-confirmed cases reported were diagnosed by about 10 percent of the local physicians, many of whom had diagnosed cases of Q fever in previous years. In many respects the failure to recognize this disease in man is similar to the situation existing when brucellosis in man was first associated with a disease of cattle. Based on present knowledge concerning Q fever, Dr. Luoto thinks it likely that human infections will become increasingly widespread and perhaps even now are occurring unrecognized.

Regardless of future implications, the presence of *C. burnetii* in animals and their products and environment should be of concern to agricultural, industrial, and public health groups. Concerted nationwide studies of the occurrence and epidemiology of the disease are needed to help define the problem, particularly as it relates to the possibility of increasing incidence of human disease.

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[1] California, Wisconsin, Ohio, Iowa, Texas, Arizona, Idaho, Oregon, Washington, Montana, Wyoming, Utah, South Dakota, Minnesota, Nebraska, Illinois, Michigan, Georgia, North Carolina, Maryland, Pennsylvania, New Jersey, New York, Connecticut, Massachusetts, Hawaii. More limited data suggest occurrence in Louisiana, Mississippi, Virginia, Colorado, New Mexico, North Dakota, Kansas, Missouri, Kentucky.

Spotted fever rickettsiae studied for immunological clues to aid diagnosis and treatment

Using a test based on neutralization by specific anti-serums of toxins produced by various rickettsiae of the spotted fever group, Dr. E. John Bell and associates of the National Institute of Allergy and Infectious Diseases Rocky Mountain Laboratory have derived information of value in diagnosis and specific prophylaxis with vaccines. Their findings were published in the Journal of Immunology.

The toxins produced by *R. rickettsii* (Rocky Mountain spotted fever) and by *R. conorii* (boutonneuse fever) could be easily differentiated, and all strains in each species were found to be similar. It was shown that the organisms of Kenya typhus, Indian tick typhus, and South African tick-bite fever are closely related to, or identical with, that of boutonneuse fever. An organism isolated from the tick, *Amblyomma americanum*, was distinguishable from all other organisms under consideration, but has some reactions which show a relationship between it and *R. conorii* and the rickettsiae of Siberian tick typhus. The rickettsia of Siberian tick typhus, with the exception of the cross reaction noted above, was also distinguishable from other strains of the group.

These results further indicate the antigenic complexity of this group of rickettsiae and provide an elegant method for differentiating the members of this family of agents which has a worldwide distribution.

Fluorescent antibody technique used to identify two tick-borne diseases

Working at the Rocky Mountain Laboratory of the National Institute of Allergy and Infectious Diseases, Drs. Willy Burgdorfer and David Lackman have used the fluorescent antibody technique in two studies at the Hamilton, Mont. laboratories, one on Colorado tick fever virus, the other on Rocky Mountain spotted fever. Their report of the identification of the virus of CTF appears in the Journal of Bacteriology. The study concerned with visualization of *R. rickettsii* by fluorescence is reported in the Journal of Infectious Diseases.

By means of homologous antibody labelled wlth fluoresceinisothiocyanate, the investigators identified 34 CTF virus isolates in suckling mice with suspensions of *Dermacentor andersoni*, the northwestern species of wood tick which transmits CTF. They also used blood samples of three species of rodents collected in nature. Control tests performed simultaneously indicate that the reactions which occurred were specific.

The fluorescent antibody technique as a means of identifying isolates of CTF virus in suckling mice is of practical value in studies on the ecology of CTF. Using this method, it is now possible to make frequent isolations of virus either from the tick vector or from the blood of rodents that serve as hosts for the immature stage of ticks. In the past each isolate had to be identified by time-consuming neutralization tests in suckling mice.

Using the same technique in another investigation, Drs. Burgdorfer and Lackman have succeeded in identifying *R. rickettsii*, the etiological agent of Rocky Mountain spotted fever, in smears of gut tissues from experimentally infected *D. andersoni*. In smears of infected nymphal ticks the organisms stained consistently with a very bright fluorescence. In those prepared from adult ticks several weeks after molting, the rickettsiae fluoresced less strongly, although they were still detectable. Experiments are in progress to determine if this phenomenon is connected with the effect of molting on the virulence of the organism, reported previously by another investigator.

(The investigators learned, upon completion of this research, that the fluorescent antibody technique has been used at the PHS Communicable Disease Center on rickettsiae of Rocky Mountain spotted fever, using individual ticks.)

In this study, all of the staining reactions, from strong fluorescence to a notably decreased amount, were specific as shown by the results of control experiments. Inhibition could be observed regularly with unlabeled immune serum, and staining was not detected when heterologous conjugate was applied or when smears of normal ticks were treated with specific conjugate. In addition, triturates of ticks found positive by the technique under study always produced clinical or serological evidence of Rocky Mountain spotted fever infection in guinea pigs. Triturates free of rickettsiae did not cause the disease when injected into guinea pigs.

Wednesday, March 29, 1961.

ARTHRITIS AND METABOLIC DISEASE ACTIVITIES

WITNESSES

DR. FLOYD S. DAFT, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

		1960 actual	1961 estimate	1962 estimate
11	Personnel compensation:			
	Permanent positions	3, 445	3, 923	4,019
	Positions other than permanent	25	40	41
	Other personnel compensation	72	57	41
	Total personnel compensation	3, 542	4, 020	4, 101
12	Personnel benefits	183	226	231
21	Travel and transportation of persons	149	213	238
22	Transportation of things	21	25	32
23	Rent, communications, and utilities	44	49	54
24	Printing and reproduction	9	9	12
25	Other services	458	934	733
	Payment to "National Institutes of Health management fund"	3,013	3, 620	4, 081
26	Supplies and materials	547	616	653
31	Equipment	316	456	526
41	Grants, subsidies, and contributions	37, 696	50, 029	51, 595
	Subtotal	45, 979	60, 197	62, 256
	Deduct quarters and subsistence charges	17	17	17
	Total obligations	45, 962	60, 180	62, 239

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	499	559	578
Full-time equivalent of other positions	6	8	8
Average number of all employees	476	482	526
Number of employees at end of year	487	531	566
Average GS grade	7. 8	8. 2	8. 2
Average GS salary	$6, 512	$7, 062	$7, 074

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Grants:			
(*a*) Research	31,022	40,859	42,425
(*b*) Fellowships	436	870	870
(*c*) Training	6,298	8,300	8,300
Total, grants	37,756	50,029	51,595
2. Direct operations:			
(*a*) Research	7,287	8,990	9,465
(*b*) Review and approval of grants	628	880	930
(*c*) Administration	186	220	249
Total, direct operations	8,101	10,090	10,644
Total program costs	45,857	60,119	62,239
3. Relation of costs to obligations: Obligations incurred for costs of other years, net	104	61	
Total obligations	45,962	60,180	62,239
Financing:			
Comparative transfers to other accounts	220	345	
Unobligated balance lapsing	680	674	
New obligational authority (appropriation)	46,862	61,200	62,239

GENERAL STATEMENT

Mr. FOGARTY. Next is arthritis and metabolic disease activities, Dr. Daft, do you have a statement for us?

Dr. DAFT. We have submitted a statement for the record. I am going to make this rather short.

(The statement follows:)

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

Mr. Chairman and members of the committee, the current fiscal year marks the 10th anniversary of the establishment of the National Institute of Arthritis and Metabolic Diseases. Last year before this committee I reviewed the remarkable growth of this Institute during its first 10 years and described to you a number of the important accomplishments of the period in our principal areas of special interest, arthritis, diabetes, and metabolism. I particularly emphasized the important role of the Congress in enabling by its steadfast support the sound development of our Institute's programs of research and of research and training grants. On March 9 of this year a special program of observance of this 10th anniversary of the Institute was carried out. On this occasion, outstanding public figures and leading scientists participated with us in a report to the Nation on "A Decade of Progress Against Arthritis and Metabolic Diseases."

In this year's statement I shall describe our current status after 10 years of vigorous growth and relate to you the Institute's most recent research and program developments. I am happy to report several highly important research accomplishments and trends, the significance of which lies primarily in the real progress which they signalize toward understanding of basic disease and life processes.

In rheumatoid arthritis, tremendous effort is being bent toward comprehension of the importance of immunologic aspects of this disease (perhaps one-third of all research in arthritis is being devoted to this approach), and increasing evidence is accumulating which suggests the possibility of an autoimmunity basis for this form of rheumatic disease. In diabetes, a large scale, carefully controlled study coordinated at seven research centers has been launched which will delineate with precision the natural history of the disease and may indicate the most effective means of preventing late complications. Also in diabetes, the finding of a new type of insulin antagonism hints at a break in the long difficulty in understanding why diabetic patients do not metabolize sugar normally even though their pancreases appear to produce insulin. In fundamental biochemical studies two extremely important accomplishments—one at Bethesda and one at Pittsburgh—have opened up new avenues of approach which should have a far-reaching effect on our biological knowledge in the years to come. Institute investigators in Bethesda have demonstrated for the first time a concrete mechanism by which hormones exert their powerful controlling effect on biological processes. In the other important advance, grantee scientists at the University of Pittsburgh have just succeeded in putting together 23 amino acids to synthesize ACTH, the pituitary hormone which stimulates the adrenal cortex to produce cortisone and other essential hormones. This substantial advance was achieved by new techniques which will be applicable to the synthesis of a number of other hormones, even custom-modified for specific desirable effects, and should open up for our understanding many aspects of endocrinology and metabolism. These are but the high spots in a most effective 10th year of life of this Institute.

The advances which I would like to describe in greater detail in the pages to follow have resulted from work done during this last year in our own laboratories in Bethesda and in the many universities, medical schools, and research institutes throughout the Nation which receive carefully weighed support from this Institute in the form of specific research grants, training grants, and fellowships.

ARTHRITIS AND RHEUMATIC DISEASES

In previous years we have indicated the extent of the human and economic losses caused by arthritis and the rheumatic diseases in the United States. More recently available figures continue to show the magnitude of the problem. At present, approximately 11 million men and women over the age of 14 are affected by these diseases. Of these, 280,000 are completely disabled and about 1,500,000 are disabled part of the time. The loss of approximately 80 million workdays, equivalent to the removal of 320,000 persons from the Nation's work rolls, is attributed to disability from arthritis and rheumatism. Latest estimate of loss to the Government in income taxes alone, because of the effect of these diseases on payrolls, is $218 million each year. The yearly cost of these diseases to the Nation in gross national product is estimated at $1,500 million. (Figures compiled by the National Health Education Committee, Inc. from Government sources.)

The actual medical and scientific effort directed against arthritis 10 or 11 years ago can be characterized as desultory. Practicing physicians had a limited armamentarium to fight these diseases, the total amount of money spent on research was a mere pittance, there was little clinical training of young physicians in the area of arthritis, and only eight medical centers in the United States had any well-defined program in this direction.

Largely due to the interest shown by the Congress and the programs supported by this Institute, the situation has become considerably more encouraging today. Under the auspices of this Institute along an estimated $9 million will be devoted this year to arthritis and rheumatic disease research. There has been a tremendous increase in professional training of young scientists and physicians in these fields, primarily as a result of the Institute's training and fellowship programs. Today, we are supporting 78 trainees in over 47 institutions. Due to this tremendous stimulus and the important activities of a voluntary agency, the Arthritis and Rheumatism Foundation, there are now more than 300 active arthritis clinics throughout the country.

Incidence of rheumatoid arthritis.—That the subject of rheumatoid arthritis, even in its gross clinical aspects, is far from well delineated has been demonstrated by a recent study concerning the distribution and incidence of the disease carried out by Dr. T. A. Lincoln of the Oak Ridge National Laboratory and Dr. S. Cobb of the University of Pittsburgh. A carefully controlled study of several hundred employees at Oak Ridge, Tenn., has supplied evidence that rheumatoid arthritis may be considerably more widespread than has been assumed heretofore. The investigation covered every employee who reported to the infirmary with rheumatic complaints. By the end of the study, 5 percent of the employees had been diagnosed as having definite rheumatoid arthritis; an additional 10 percent satisfied practically all criteria for the disease and were classified as probably having rheumatoid arthritis. The investigation found that the longer the "probable" patients were observed, the greater was the percentage of those who eventually displayed complete symptomatology of the disease. It was also found that a very high proportion of "probable" subjects who had only mild joint symptoms, and who ordinarily would never have been considered rheumatoid arthritis patients at this point, had rheumatoid factor blood tests which were quantitatively between the negative findings characteristic of normal, healthy individuals and the positive tests obtained in the case of full-blown clinical cases. On the basis of this significant study it appears that rheumatoid arthritis is much more common than has been assumed in the past. In contrast to the more severe cases usually seen in clinics and consulting rooms, there seems to exist an additional reservoir of afflicted subjects whose cases may run a relatively benign, remittant course.

Arthritis and immunologic mechanisms—As the committee is aware, the goal of the research effort of this Institute is to find the basic causes of rheumatoid arthritis in order to enable us to attack or prevent the disorder proper and not merely its symptoms. With this in mind, the question of the role of autoimmunity in the causation of rheumatoid arthritis is receiving vigorous research attention

In recent years it has become an increasingly plausible hypothesis that rheumatoid arthritis results from a state of hypersensitivity, and quite possibly, from autosensitivity or autoimmunity. According to this concept it is possible for an individual to become sensitive (or "allergic") to substances normally present in his body tissues and to produce protective antibodies (protein substances which provide immunity to specific noxious agents) against these substances (antigens). The resultant antigen-antibody reactions in the various tissues are thought to lead to the pathological changes characteristic of the disease.

In last year's report to the committee I mentioned the unique "rheumatoid factor(s)" found in the serum of patients suffering from rheumatoid arthritis, and that it has been made use of as a diagnostic tool in a number of tests developed for the disease in our own laboratories or by our grantee scientists. I further indicated that a number of studies had suggested that these factors resulted from a hypersensitivity phenomenon. As has now been more fully established, these factors have many characteristics of true antibodies and an intensive search is now underway to establish the nature of the postulated antigen, the identity of the deleterious substance to which the body may be sensitive (in response to which the rheumatoid factors are presumably produced). A prevalent speculation holds that this substance may become antigenic, or antibody-arousing, only after undergoing certain alterations, as an aftermath to an infectious process, for instance, or due to some innate defect in body metabolism, characteristic for the rheumatoid patient.

A group of grantees of the Institute at the Hospital for Special Surgery-Cornell Medical Center in New York has succeeded in developing a new extremely sensitive method which specifically stains the rheumatoid factor and permits its detection in tissue slides. This technique is so sensitive that it detects the presence of rheumatoid factor in situ even in cases where the more conventional hematologic methods fail to demonstrate rheumatoid factor in the patient's blood. Using this method the investigators were successful in detecting and specifically demonstrating the presence of the rheumatoid factor in biopsy material obtained from lymph nodes and inflamed joints of adults and children with active rheumatoid arthritis. It is believed that this study has demonstrated the site of production of rheumatoid factor, in the acurely inflamed joint linings, and provides further support to the idea that these factors are true antibodies.

A hitherto undetected, new "factor" has been found in the blood of rheumatoid arthritis patients by another group of grantees at the Hospital for Special Surgery-Cornell Medical Center in New York. As reported by these investigators, this substance is distinctly different from the known rheumatoid factor; it interferes with the normally prompt interaction of the complement system with antibody-antigen complexes. (Complement is a complex protein formed in the blood which aids in the removal from the body of foreign and toxic substances previously neutralized by specific antibodies.) The "Inhibitor of Complement Fixation" was also recovered from patients with systemic lupus erythematosus and scleroderma, two diseases in which the damage to connective tissue is similar to that found in rheumatoid arthritis. These studies are continuing with the view to clarifying the role of the new factor in the etiology of the rheumatic diseases and its interrelationship with previously found blood factor(s) in rheumatoid arthritis.

Sjögren's syndrome.—A recent study in our clinical center has added additional fitting pieces for the jigsaw puzzle of the rheumatic diseases and provides further support for the concept that immunologic mechanisms may possibly constitute the underlying cause. Scientists at our Institute have made a systematic serological study of patients with Sjögren's syndrome, a disorder characterized by hypofunctioning of the tear and salivary glands and, in many cases, by rheumatoid arthritis. The comprehensive serological investigation showed that these patients displayed an abnormal immunologic reactivity; almost all responded positively to the bentonite flocculation test and sheep cell agglutination test for rheumatoid arthritis although only one-third had definite clinical signs of the disease. Other specific humoral antibodies against the patients' own tissue components were also found. These findings suggest that a deranged immunological mechanism involving an autoimmunization phenomenon may be the basis of the pathogenesis of Sjögren's syndrome. Since this disorder is frequently associated with rheumatoid arthritis or other connective tissue diseases (such as scleroderma or systematic lupus erythematosus) these findings appear to strengthen the trend of thought which connects the cause of rheumatic disease with immunologic mechanisms.

This year we are making an important extension of the Sjögren's syndrome study. In an unusual effort to include many more patients and to bring the research laboratory to families of previously studied patients whenever the latter are geographically unavailable to the research laboratory, a senior investigator from this Institute has been sent to selected regions in the United States with a uniquely equipped, completely self-contained mobile trailer. This trailer laboratory provides completely independent research laboratory facilities including X-ray machine, centrifuges, refrigeration, and a 3,000-watt generator. The study attempts to elucidate familial and geographic aspects of Sjögren's syndrome to add to our basic understanding of the rheumatic diseases. Among others, completely inbred Indian tribes are being investigated since they offer to the investigation undisturbed familial bloodlines.

A wealth of accumulated data from all over the Nation, from the Black Feet Reservation in Montana to the Papago Indians of Arizona, from the Carolinas to California, are presently being processed and evaluated and we expect that considerable light will be thrown by this continuing study on the influence of inheritance as well as climatic conditions and geography on susceptibility to and incidence of the rheumatic diseases.

Treatment with steroid hormones.—The prominent mention in this report of studies on the immunologic aspects of rheumatoid arthritis, as well as its incidence and familial and geographic distribution, should not overshadow the painstaking day-by-day clinical research devoted to evaluation of new anti-inflammatory and analgesic drugs carried out both by grantees and investigators at Bethesda. This important work continues hand in hand with development of new methods of physical therapy and rehabilitation for advanced cases of the disease, and with the intense efforts to determine the significance of immunologic mechanisms.

In the course of this work clinical investigators of this Institute, in collaboration with the National Institute of Neurological Diseases and Blindness have discovered a heretofore unnoticed, but relatively infrequent side effect of long term corticosteroid therapy—production of slight opacities in the lens of the eye. In most cases, this particular type of opacity, posterior subcapsular cataract, causes no impairment of vision, rarely requires surgery and should not be considered an alarming or major hazard of vision.

DIABETES

Here again, as in the field of the rheumatic diseases, it is the multifaceted, diverse research activity of a wide spectrum of investigators from biochemist to clinician, from enzymologist to endocrinologist, which must carry the fight against diabetes. They are making steady progress toward determination of the chemical nature, the physiologic role, and the molecular configuration of enzymes and hormones, and toward understanding of the pathologic responses of cells and tissues through which it will be possible to arrive eventually at the root of this disorder.

As we have previously described, this best known and most important of the metabolic diseases appears to result from insufficient insulin production or action in the individual's tissues. Because of this abnormality, which is due to an inherited predilection, the diabetic patient is unable to utilize properly carbohydrates (sugar) so that excessive amounts of glucose accumulate in the blood and tissues and spill over into the urine. The committee has previously indicated its understanding that far from being as simple as the foregoing sounds, diabetes is an extremely complex disorder which is known to involve concurrent abnormalities in the body's fat and protein metabolism.

Clinical studies.—While unsolved questions related to the fundamental causes of diabetes are under unabated investigation by teams of our scientists and grantees, others are engaged in closing gaps in our knowledge concerning the clinical aspects of the disease. During the last few years it has been possible to lighten the burden of therapy-by-injection for hundreds of thousands suffering from diabetes and to extend to many a satisfactory measure of control through the medium of the new oral hypoglycemic drugs. These new oral antidiabetic agents continue to be subject to extensive clinical evaluation by scientists and grantees of this Institute.

Results of new studies have thrown additional light on the mode of action of these drugs. One widely held theory described to the committee in previous reports is that the drugs stimulate the beta cells of the pancreas, the normal site of synthesis of insulin, to release maximal amounts of this hormone, the absence or inadequate action of which is the evident defect in diabetes. It is conceivable that prolonged stimulation of the pancreatic beta cells by use of an oral antidiabetic drug could lead to their eventual exhaustion and atrophy. Experimental evidence now obtained by grantee investigators at the University of Chicago and the Chicago Medical School, working with animals, indicates that this is apparently not the case. However, extensive clinical evaluations carried out by grantee scientists at Georgetown University Hospital have turned up increasing evidence that individual patients may become resistant to one or more of the oral drugs and that the percentage of secondary failures (failure of hypoglycemic action after a particular drug originally proved efficaceous in controlling the patient's diabetes) may increase with more prolonged oral drug therapy.

A particularly important new study approach in the field of diabetes should be communicated to the committee at this time. Under the support of this Institute, the first large scale, carefully controlled and long term study of the natural history of diabetes in individuals is now in its pilot stage at seven research institutions located throughout the country. It is anticipated that this well-organized broad study will go far toward solving the long-debated question of the best therapeutic regimen for prevention of diabetic complications. The study should also ultimately throw significant light on the mechanism of action of both insulin and of the oral drugs. This new "university group diabetes study" is investigating the incidence and severity of late diabetic complications such as retinopathy, atherosclerosis, and kidney and nervous system disorders in large groups of reasonably controlled patients treated according to selected methods of therapy. The complications of diabetes have long been of great concern to the medical profession since it is the complications which directly shorten the patient's life span and disable him prematurely. (For instance, diabetes is numerically the most important cause of blindness in the United States.) This interregional investigation is designed to determine the rate of development and severity of the complications of the disease and the long-term influence of four different methods of therapy on their appearance and progression. The four methods of treatment under study are: (1) diabetic diet, (2) diabetic diet and the oral drug tolbutamide, (3) diabetic diet and insulin, the dosage being adjusted to maintain control of blood sugar levels, (4) diabetic diet and a fixed dosage of insulin administered on the basis of the patient's body weight.

Approximately 700 patients, 100 at each center, are included in the study; these are freshly diagnosed diabetes patients who have never been previously treated for their disease. This long-term study involves seven principal investigators, an eminent epidemiologist and 25 associate investigators. It is expected to produce most significant contributions to our fight against diabetes and could very well become a prototype for similar large scale, interregional, cooperative clinical trials in other diseases.

Blood vessel complications—New pathological lesion.—The vascular complications of diabetes, such as retinopathy leading to blindness, and arteriosclerosis leading to gangrene of the extremities and a very high rate of coronary heart disease, present a most serious problem in the management of diabetes. They are extremely important because by far the most frequent mode of death in a diabetic patient today is by way of a vascular complication. It has been commonly thought that the vascular complications are due to an abnormally speeded up process of atherosclerosis in diabetics. A potentially very important discovery which may clarify the cause of the dangerous vascular complications of diabetes has recently been announced by a grantee investigator at the Jewish Hospital in St. Louis. This investigator and his associates have found a new and unique type of proliferative lesion in the lining of the small blood vessels in the major organs, extremities, and eyes of diabetics. This lesion does not contain the fatty substances which are characteristically involved in the conventional process of atherosclerotic narrowing of blood vessels. In contrast, these proliferative lesions have many of the histologic or microscopic characteristics of lesions previously associated with such diseases as rheumatic fever and glomerulonephritis. Histologically this picture resembles lesions which have been produced experimentally by a variety of immunogenic mechanisms, and these grantee investigators believe that hyperimmunity may indeed be a factor in diabetic vascular disease. Based on these very provocative findings, further studies are now being carried out to determine what immunologic reactions are taking place and what the full significance is for the cause of diabetic vascular complications.

Studies of fundamental processes.—Important studies are proceeding on the fundamental mechanisms which operate in this metabolic disease: The manner in which the key hormone insulin acts, its specific target-tissues, and correlations of insulin dysfunction with fat and protein metabolism. Particular attention is being devoted to further understanding of an apparently important function of insulin, to facilitate the transport of glucose across cell membranes so that energy-yielding blood sugar can enter body cells. A useful adjunct to these studies has been recently devised by development of improved methods for measuring insulin and insulin inhibitors in the blood. The amount of insulin necessary for its normal hormonal activity in tissues is extremely small and its precise measurement, an essential for progress in this basic research, has posed a problem which has never been fully solved before. By modifying an older assay method which involved rat diaphragm muscles, our scientists in Bethesda have now made it possible to assay human serum for much smaller quantities of insulin-like activity than has previously been possible. Still newer techniques are being developed for this task and promise to supply greatly needed information about mechanisms of insulin action and resistance and the sites of insulin activity in the various tissues. A new fluorescent technique has been developed in our laboratories which makes minute amounts of insulin distinctly visible under the microscope and promises to permit us to follow the fate of this hormone within individual cells.

Insulin antagonism.—A particularly important investigation in this direction has been recently reported by clinical investigators in Bethesda. It concerns the discovery of a hitherto unknown type of insulin antagonism found in diabetic patients who have never been treated with insulin before. The likelihood that the fundamental defect in diabetes might be caused by substances in the patient's body which interfere with provision of an effective insulin concentration to muscle tissues has been considered by endocrinologists for many years. In the past our own scientists and outside investigators have found inhibitors or antagonists to normal insulin action which have the properties of antibodies elaborated by the body in protective (immunological) response to administered insulin introduced to the body during the course of insulin therapy. Such insulin resistance may be theoretically expected and has been established in a number of patients; it is particularly marked during diabetic acidosis or with severe infections. The results of our latest investigation, however, differ from these previous observations in that an insulin-inhibiting substance was detected in the plasma of diabetic patients who had never been treated with insulin before; therefore, this antagonist cannot represent an antibody elaborated in response to administered therapeutic insulin. This new insulin-inhibiting substance could no longer be detected once the diabetic symptomatology of these patients was under control. The possibility exists that this new antagonist is a hormone of pituitary origin, perhaps related to the growth hormone. Results of this study shed a provocative light on an important likely cause of diabetes other than the original theory of pancreatic inability to produce insulin.

GASTROENTEROLOGY

Gastroenterology is a relative newcomer to the realm of responsibility of the Institute. Nevertheless a number of specific new findings, related primarily to increased fundamental knowledge on the physiology of the gastrointestinal tract, testify to the productiveness of efforts of our scientists and grantees during the last year. Diseases of the gastrointestinal tract under investigation run a gamut from widely known disorders with a tremendous national incidence like peptic ulcer to relatively obscure ones like idiopathic steatorrhea, and include a vast array ulcerative colitis, regional ileitis, intestinal malabsorption, and many others. As we have stated previously to the committee, the importance of gastrointestinal disorders in the national health picture cannot be emphasized enough; it is reflected in the fact that diseases of the digestive system rank second only to heart disease in the frequence of illness requiring attendance by a physician.

Gastroenterology today offers almost unparalleled opportunities for significant research activity. In gastroenterology the fundamental sciences of medicine and the art of healing are indivisibly combined. Diseases of the digestive system encompass many problems of internal medicine and important aspects of surgery. These diseases are only beginning to receive the research attention they deserve for in the past too few investigators were interested in them, and gastroenterology tended to be a relatively narrow specialty. The renewed and productive interest in the gastrointestinal area since it became subject to vigorous research support, together with a major expansion in the variety of disciplines from which problems in gastroenterology can now be approached, may be expected to bring forth valuable contributions to understanding of the various relevant disorders and to result in practical approaches toward their prevention and cure.

Peptic ulcer.—A particularly active group of grantee investigators at the Northwestern University Medical Center has recently contributed considerably to our knowledge of ulcer pain. Heretofore it has been a commonly accepted belief that the nagging and sometimes excruciating pain of peptic ulcer, so familiar to many Americans, is caused by direct chemical irritation of the denuded ulcer area of the intestinal inner wall by hydrochloric acid present in gastric secretions. Studies of more than 500 ulcer patients by these investigators have now shown that ulcer pain is apparently the direct result of a disturbance in motor activity of the stomach and duodenum. A variety of techniques were used in this investigation. One was the "acid test," in which hydrochloric acid was instilled into the stomachs of patients with active ulcers and during which only one-third of the subjects developed pain. Another technique involved use of a new fluorocinematographic apparatus, developed especially for this investigation, which enabled the investigators to make X-ray motion pictures of gastrointestinal motor activity in ulcer patients during periods of pain, while concurrently intraluminal pressure changes in various parts of the stomach and duodenum were recorded and correlated with the gastric motility. This group of investigators has now concluded that ulcer pain is a direct result of disturbed motor function of the stomach. This finding facilitates a new approach to effective drug palliation and therapy in this common disorder.

Esophageal sphincter mechanism.—During the last year, two groups of grantees, working independently, one at the University of Virginia and one at Northwestern University, have succeeded in elucidating the long-disputed mechanism by which food in the stomach is prevented from returning upward through the esophagus during digestion. The exact nature of the closing mechanism at the upper end of the stomach has been a matter of dispute since the 18th century. Using the apparatus mentioned above which permits the simultaneous taking of fluoroscopic motion pictures of the esophagus in action while measuring the intraluminal pressures at various portions of the esophagus and stomach, the Northwestern University group has demonstrated that the lowermost inch of the esophagus, although not composed of anatomically distinct muscle fibers, acts as a physiological sphincter (functional closing mechanism) through a bundle of circularly arranged muscle fibers. These NIAMD-supported clinical investigators were able to map the exact location of this functional sphincter—a matter of considerable importance since it affects the surgical treatment of patients with benign or malignant disorders of the gastroesophageal junction. A serious problem in such patients after surgery is refluxing of stomach contents into the esophagus if the muscle bundle which normally acts as the closing mechanism has been divided or excised by the surgical intervention.

Concurrent with these investigations the group of grantees at the University of Virginia was able to confirm the Northwestern results through surgical studies with experimental animals. When the sphincter segment of the esophagus was surgically isolated or removed, there was a loss of reflux control; this control returned when the esophageal segment was restored to its normal position. These surgical researchers also designed an operation which offers great promise as a reconstructive measure in patients who have lost sphincteric function in the lower portion of the esophagus through surgical intervention for various causes. They have devised the building of an artificial extrinsic sphincter by wrapping a flap of diaphragm muscle around the surgically reconstructed esophagus where it joins the stomach. Respiratory motions then cause this flap to close off the stomach and give an acceptable measure of sphincteric control.

New simple test for liver disease.—An NIAMD-supported scientist at Harvard University has developed a new, relatively simple test which provides a sensitive index of the severity of existing liver disease. The test also indicates presumptive presence of esophageal varices, hemorrhage-prone varicose veins of the lower end of the esophagus, which constitute a not uncommon and occasionally hazardous complication of longstanding liver disease. This new diagnostic procedure consists of feeding the patient a provocative dose of a simple salt, ammonium citrate, and then measuring resultant levels of blood ammonia. Patients with severe liver disease can be distinguished by a characteristic hyperammonemia which persists for many hours. In contrast, patients with normal livers or well-compensated liver disease show no appreciable rise in blood ammonia levels, provided esophageal varices do not exist. Presence of esophageal varices is revealed by a rapid rise in blood ammonia levels followed by a rapid fall. The procedure is safe and in many instances has been proved more accurate in defining presence or absence of esophageal varices than radiographic techniques on which physicians have had to rely exclusively heretofore.

DISEASES OF METABOLISM

One of the most important areas of responsibility of this Institute is that of the diseases of metabolism, disorders in which in one or more various ways defects occur in the biochemical processes by which the body carries out its great number of tasks. These tasks include the synthesis of appropriate amounts of endocrine hormones, absorption and excretion of a variety of inorganic chemical elements and of useful foodstuffs, and, by a multitude of intermediate chemical processes, the need for individual cells to extract or make over various substances for energy for growth and work. Metabolic diseases thus include conditions in which there is an excess or inadequacy of one of the endocrine hormones, as in hypothyroidism or Cushing's syndrome, disorders like gout in which there is either overproduction or underexcretion of uric acid, and complex diseases like diabetes in which there is both inadequate handling of sugar and abnormalities in fat metabolism as well.

Scientists receiving our support are making significant headway in this area in recent years by attacking particularly those diseases in which it is suspected that the metabolic defect is a single one or in which the defects tend to reveal their nature by being so severe as to threaten life at an early age. In these disorders, termed "molecular diseases," it has been possible to bring fundamental research at the cellular level closest to the clinic (or the patient with disordered metabolism closest to the laboratory, depending on the point of view), and apply research techniques in enzymatically controlled cellular processes directly to clinical investigation. In these molecular diseases the failure of elaboration of a specific protein with a unique metabolic function, or lack of a specific enzyme, poses a biochemical block to the orderly completion of basic chemical reactions which are prerequisites to healthy cell, tissue, and body function. Moreover, accumulating abnormal products of the altered metabolism almost invariably prove toxic to the afflicted organism and cause progressive, irreversible, and sometimes ultimately fatal damage.

The past year has seen a number of significant advances in our knowledge of the metabolic and molecular diseases which have issued from laboratories of grantee scientists or from our Institute. Some of these are enumerated herewith.

Wilson's Disease.—Wilson's disease is an ultimately fatal familial disorder caused by the body's inability to limit absorption and effect excretion of copper contributed by the diet. It is characterized by progressive accumulation of copper in vital organs (particularly the brain and liver) with concurrent, irreversible toxic damage. Two grantee investigators of this Institute have developed a prophylactic regimen for Wilson's disease which has produced encouraging results. This treatment is based on provision of a copper-poor diet immediately after presence of the disorder is suspected. A fixed quantity of potassium sulfide is given with each meal in an effort to precipitate any dietary copper and make it unavailable for intestinal absorption. In addition, these investigators found that daily administration of penicillamine (a metal-binding agent) facilitates urinary excretion of absorbed copper. With the aid of this regimen it has been possible to bring about definite clinical improvement in a number of patients in the advanced stages of the disease and to prevent onset of clinical symptomatology where the diagnosis was made early in life before toxic damage has occurred. Simultaneously, one of our scientists in Bethesda has succeeded in developing an effective, simple, and rapid blood test which permits mass screening of apparently healthy children to detect those who have the disease before clinical symptoms are apparent. Symptoms usually appear after the age of 6 years, and for a few years thereafter the grantee-developed prophylactic regimen can still prevent the ravages of this disease if it is prescribed.

Galactosemia.—Other important advances concern galactosemia, an often fatal congenital molecular disease of infancy and childhood on which we have made several previous reports to this committee. Inability to metabolize galactose, a component of milk sugar, you will recall, brings about a toxic condition which leads to the development of cataracts, jaundice, progressive mental retardation, and early death. Five years ago I reported to the committee that the causative metabolic mechanism underlying this disorder had been elucidated by a cooperative intralaboratory effort at our Institute and that a simple test for the detection of the disease had been worked out. Recently scientists in our laboratories have devised a means of maintaining control of the quality of dietary treatment by developing a sensitive test for galactose 1-phosphate in the patient's blood, a compound thought to be the most important toxic agent in the disease. This test will aid in monitoring the prescribed diet of these children to insure that they are completely free of milk and milk-containing foods. This is important since it is difficult to find processed foods which do not contain milk derivatives, and the clandestine ways children have of getting food often result in unsuspected breaks in their prescribed, health-maintaining diet. The reagents for this new diet-monitoring test are now commercially available in the form of a diagnostic kit.

Further hope for increasing our armamentarium against galactosemia has been furnished by additional recent developments. Two years ago we reported that scientists in our laboratories had shown that the steroid hormone progesterone would facilitate metabolism of galactose; this was found in test tube preparations of the biochemical process utilizing a patient's serum. Since then our scientists have shifted their study to patients and have found that administration of progesterone and of menthol (the substance responsible for the characteristic odor of peppermint) can enhance the ability of galactosemic patients to metabolize galactose. The action of both compounds must be carefully evaluated further before practical therapeutic benefits can be claimed. Though progestoerone or menthol therapy is not expected to replace the present management of galactosemia at this point, they may well be used in the future when patients are acutely ill as a result of ingestion of high milk diets or during exacerbations when cataract development and mental retardation seem to be overwhelmingly and rapidly progressive.

Osteoporosis.—Osteoporosis is another metabolic disorder which has been subject to a well conceived fundamental clinical and laboratory investigation in our Institute. Postmenopausal or senile osteoporosis is one of the chief causes of a variety of fractures and compression deformities which beset a considerable percentage of our older citizens. The disorder is characterized by a gradual "thinning out" of individual bones; they become less dense (porous) and gradually lose their normal structural rigidity. The bones most commonly affected are those of the spine and pelvis; the disorder is frequently seen as a thinning of individual vertebra of the lower spine followed by compression deformities or outright fracture and collapse. This is accompanied by a chronic low back pain and frequently leads to deformity of the spine, progressive shortening of stature, and functional disability. Moreover, osteoporosis, by virtue of the weak, porous bones which it produces, sets the stage for most of the fractures which victimize the elderly since it predisposes to ready breakage even under relatively minor mechanical stress. Thus it may be perceived as the true etiology of the numerous broken hips which hospitalize so many oldesters for prolonged periods and in many cases initiate their physical decline and eventual demise. In brief, osteoporosis is one of the major causes of physical disability in old age, especially in women, and in this respect ranks closely behind the arthritides.

To date it has been a generally accepted postulate that this disorder is caused by the gradual deficit in anabolic female and male hormones which accompanies menopause and old age. Bone tends to erode slowly as a consequence of obligatory excretion of calcium by the kidney. Normally, in the presence of ample anabolic hormones, compensatory new bone is laid down at points of stress, but the osteoporotic, who is deficient in tissue-building steroid hormones, cannot regenerate his thinning bones—and eventually suffers the consequences. Fundamental investigations in our laboratories have begun to throw a new light on the causation of this disorder. Another additional factor, previously largely dismissed by the mainstream of clinical thought, appears to be involved—namely the long-term balance between incoming, dietary, and outgoing, urinary and fecal calcium in the individual. As the result of studies with radioisotopic calcium by Institute scientists, it has been found that during the process of continual erosion and regeneration of bone about one-fifth of the calcium, the component which confers on the skeleton its structural rigidity, is normally lost and replenished every year. All adults lose varying amounts of calcium via urine and feces; these daily losses must be compensated with new calcium from food and drink. If over a period of many years the supply of new dietary calcium is insufficient, the individual's skeleton is likely to become progressively demineralized. The results of metabolic balance studies in Bethesda now suggest that the calcium requirement may vary widely from one individual to another and hint that in patients who develop osteoporosis the requirement may either be higher than for normal individuals or higher than the patient's customary intake over many years. These studies support the long-neglected hypothesis that dietary calcium at abundant intake levels throughout the adult and advanced years probably plays an important role in the integrity of the skeleton of the aging and in the prophylaxis of osteoporosis.

Cystic fibrosis.—Last year I informed the committee about the organization of a new Pediatrics Metabolism Branch at Bethesda, under the direction of Dr. Paul A. di Sant'Agnese, with the primary mission of investigating cystic fibrosis. From previous testimony, the committee is well aware of the characteristics of this hereditary disease of children and adolescents, involving a generalized malfunctioning of the mucus, sweat, and related exocrine glands. At present, a vigorous research effort, which so far has involved 51 patients, is proceeding in the Bethesda laboratories and Clinical Center.

The principal aim of the investigation is to elucidate and, if possible, uncover the basic defect in mucopolysaccharide metabolism presumably responsible for the abnormal secretory activity accounting for the clinical manifestations of the disease. Pathways of biosynthesis of mucoproteins are now under investigation and the composition of body secretions from cystic fibrosis patients is being studied with special emphasis on factors which may influence the solubility, physical characteristics, and susceptibility to precipitation of their abnormal mucoid components. Simultaneously the abnormally high salt level in the sweat of cystic fibrosis patients is being studied quantitatively under different conditions of stress in an effort to correlate the intensity of this disease manifestation with the extent of the hereditary "load" (or quantitative inherited disease potential) carried by the individual. In the course of this work, our investigators have found that patients who have inherited a full disease potential from both parents ("homozygous" patients) cannot reduce their high sweat salt levels even under conditions of extreme salt deprivation and when supported with steroid hormone therapy. On the other hand, patients who have acquired the hereditary endowment for cystic fibrosis from one parent only ("heterozygous" patients) are able to conserve salt under these conditions and therefore survive better in hot weather. In cystic fibrosis severe heat loads may lead to possibly fatal "heat exhaustion" in nonsalt sparing patients.

In the course of these investigations new understanding has been gained on the extent to which the degree of clinical disorder is determined by the number of impared genes in the patient's hereditary makeup. Twenty to thirty percent of relatives of cystic fibrosis patients have been shown to have abnormally high salt levels in their perspiration, and thus exhibit a partial manifestation of the disease. Evidence has also been obtained that some adults who suffer from chronic pulmonary infections also have high sweat salt levels. It is postulated that they may be individuals with a previously unrecognized, partial hereditary endowment for cystic fibrosis who did not develop all the manifestations of the disease to their fullest extent in childhood, and have thus managed to reach adult age.

In addition to this work of our scientists in Bethesda, 30 research project grants have been authorized this year for studies on cystic fibrosis at research institutions elsewhere.

NONCLINICAL RESEARCH

The scientific advances described in this report have been categorized under various disease headings. This was done primarily for the convenience of the committee and not because of any real separation between the fields as far as fundamental knowledge is concerned. As research progress continues, it becomes increasingly evident that underlying all the fields of biology and medicine is a substructure of fundamental knowledge common to all the preclinical and clinical sciences. Obtaining this basic knowledge is one of the prime activities of the National Institute of Arthritis and Metabolic Diseases.

Despite the gratifying progress which is being made in controlling some of the important diseases with which we deal there is still far too little known about their fundamental cause and nature. Much of this needed knowledge must come from basic research, from the elucidation of the fundamental physical, biochemical, and physiological facts which make up the basic fabric of all the biological and medical sciences. The additions to our basic knowledge are permanent foundations upon which the scientists of the future may build additional advances both in the pure and applied fields. In such terms, orderly, practical benefits accrue from fundamental research almost inevitably even though they were not necessarily anticipated when the original quest was undertaken.

The basic research program of this Institute extends over a vast area encompassing the fields of biochemistry, biophysics, enzymology, physiology, pharmacology, pathology, nutrition, endocrinology, histology, toxicology, photobiology, and others as they relate to life processes in health and disease. The studies undertaken include research with germfree animals, inquiries into the metabolic problems of obesity, elucidation of the action of vitamins and hormones, exploration of the function of cell components which determine heredity, and many other investigations. The following are merely two specific examples of this very extensive basic research effort.

Mechanism by which steroid hormones regulate metabolism.—Studies conducted during the recent year in our laboratories in Bethesda have indicated a mechanism by which steroid hormones dramatically influence the direction or strategic biochemical cell reactions: toward energy-yielding chemical breakdown ro toward cell-building protein synthesis. Heretofore the profound influence of hormones in regulating enzymatic catalysis of chemical reactions was well known but little understood. Previous studies by other investigators had suggested that hormones exert any direct biochemical influences by participating chemically in the metabolic reactions. Investigators from our Institute have now established that certain steroid hormones exert their influence by directly altering the molecular structure of a key enzyme in cell metabolism by fragmenting it into four smaller molecules, catalytically inactive for the original metabolic reaction.

These investigators found that diethylstilbesterol, estradiol, and progesterone (all belonging to the group of so-called female hormones) can inhibit by their presence an important enzyme of intermediary body metabolism, glutamic dehydrogenase. Ordinarily this enzyme facilitates the energy-yielding chemical degradation of glutamic acid (an amino acid or basic building block of proteins). In the absence of this enzyme, or when it is inactivated, the scales are tipped toward the accumulation of glutamic acid and its incorporation into protein molecules synthesized by the cell. This study, while appearing on the surface to elucidate only a single facet of cell metabolism, may be of momentous import and may well exert considerable influence on the direction which basic biological research in this area will take in the future. At present it serves as the first specific demonstration of an important way in which molecular biologic mechanisms may regulate the most basic life processes. Thus, the presence or absence of a specific hormone, through direct fragmentation and consequent inactivation of an enzyme in a key metabolic position determines the direction which the cell's life processes will take: on one hand, energy-yielding degradation of foodstuffs, on the other, protein synthesis and indirectly, cell growth and cell proliferation.

First successful synthesis of ACTH.—One of the most outstanding achievements in fundamental research during the decade of the Institute's existence has been the recent, successful laboratory synthesis of the cortisone-releasing hormone ACTH (adrenocorticotropic hormone) by a team of grantee biochemists at the University of Pittsburgh, under the direction of Dr. Klaus Hofmann. ACTH is a hormone produced by the pituitary gland, the body's "master gland," which directly produces hormones essential for normal life processes and indirectly coordinates the production of other hormones in other organs throughout the body. ACTH causes the cortex, or outer shell, of the adrenal glands to release cortisone and other essential steroid hormones into the circulation and thus the system at large.

Until now the only ACTH available for therapy or scientific investigation was that produced naturally by animals or humans. The new synthetic hormone, which has the full biological activity of natural ACTH, represents the largest proteinlike molecule yet reproduced synthetically by man. This group of investigators constructed the synthetic hormone by putting together 23 natural amino acids, the building blocks of all proteins. The tedious chemical procedures used in the process, many of them originally devised by Dr. Hofmann's group, are expected to pave the way for synthesizing even more complex protein-like molecules of biological importance.

According to the investigators, the processes developed by this group are adaptable to producing the synthetic hormone in significant quantities on a larger-than-laboratory scale. Production of this synthetic, biologically active ACTH culminates 7 years of efforts of this group of the University of Pittsburgh and 17 years of investigation by scientists throughout the country. Although the full significance of this outstanding achievement will only unfold in the future, the investigators suggest that it will help to clarify the all-important functions of the pituitary gland, that it will allow medical scientists to work with pure ACTH of known standard composition, and that it may lead to an understanding of how the pituitary gland stimulates the adrenal cortex to produce cortisone and other important steroid hormones. Moreover, the techniques developed for this synthesis can now be used to develop modifications of the natural ACTH molecule in the hopes of producing structurally related compounds which possess specific desirable characteristics of ACTH and are devoid of some of the undesirable side effects of the hormone.

The history of ACTH research goes back to 1943 when crude ACTH, a protein with a molecular weight of approximately 20,000, was isolated from animal pituitary glands for the first time. Since then different groups of investigators have established a structural sequence of 39 amino acids for the natural ACTH molecule and determined that the first 24 amino acids constituted the portion of the molecule which is responsible for the profound biological powers of this hormone. The group of grantee scientists in Pittsburgh started building molecules from individual amino acids soon thereafter. Early this year, this team synthesized a 16-unit molecule, but it still had only one-thousandth of the activity of natural ACTH. Now, this group has succeeded in obtaining 100 percent biological activity (verified independently through biological assays conducted in another laboratory) with a molecule containing 23 amino acids and a molecular weight of 3,200.

PROGRAM NOTES

Other diseases of relevance for which this Institute is providing research support or which are being investigated by our scientific staff include the various forms of hepatitis, diverse hematologic disorders, burn shock, sprue, and many other afflictions. Gradual growth of our research grants programs has resulted in increasing recent attention to three disciplinary areas of clinical medicine, pediatrics, dermatology, and orthopedics, in addition to our traditional emphasis on support in many aspects of internal medicine and surgery.

At Bethesda we are extending our efforts in physical biology, the area of laboratory research concerned with physical and material features, aspects and characteristics of life processes. As outlined in previous reports, this field deals with the interrelationship of molecular, cellular and organ structure to function; it strives to illuminate the interconversion of energy and structure as influenced by environment, both immediate and relatively remote. Since this field is becoming increasingly concerned with the vital features of molecular structure, this Institute is organizing a new group of scientists under the proposed title of Laboratory of Molecular Biology. In this laboratory the ideas and skills of the crystallographer and spectroscopist will join those of the enzymologist and geneticist in painstaking biological dissection of macromolecules, such as nucleic acids and proteins. [Laboratory space for this group is in the advanced planning stage, but availability awaits completion of the new building of the National Institute of Dental Research. Movement of dental investigators will then permit renovation of an existing laboratory building assigned to this Institute.] We are confident that from this new association of diverse technical backgrounds accomplishments of substantial merit and value will result.

Civilian Nutrition Surveys.—Last year I apprised the committee of our participation with the Department of Defense, the State Department, the Department of Agriculture the Atomic Energy Commission, and the International Cooperation Administration, in the nutrition survey activities of the Interdepartmental Committee on Nutrition for National Defense (ICNND). Up to that time surveys had been carried out in 11 countries in Asia, Africa, and South America. During the past year extensive nutrition surveys were conducted.in Thailand, Chile, and Colombia. In contrast to surveys conducted in previous years, which were oriented primarily toward the defense forces of thr respective countries, greater emphasis was placed on the nutritional status and nutritional needs of the civilian population in the areas surveyed, where malnutrition has economic as well as health implications. It may interest the committee that the survey team was at work in Chile when the calmitous earthquakes of 1960 occurred, and the team actively participated in disaster relief work. This assistance created considerable local good will and resulted in a number of official expressions of appreciation. In 1960, data collected during an earlier survey in Vietnam were processed and specific remedial recommendations were made to the Government of the Republic of Vietnam. At this very moment another survey is underway in the Republic of Lebanon.

The work of ICNND is of value not only to the countries where nutrition surveys are conducted, but it has become increasingly valuable to the National Institutes of Health and various other institutions in the field of health and medical research. One of the most direct benefits has been the training of personnel in clinical nutrition; in addition, our Institute has been able to extend considerably its knowledge of nutritional diseases associated with dietary deficiencies prevalent in the population surveyed.

Fifth International Congress on Nutrition.—Since nutrition has been traditionally in the realm of responsibility of this Institute I would like to mention briefly an important program in which the Institute participated this year. Over 2,000 scientists from 65 nations attended the week-long Fifth International Congress on Nutrition opened by the President of the United States on September 1, 1960, in Washington. The Congress, the first held in the United States, was sponsored by The International Union of Nutritional Sciences, The American Institute of Nutrition, and The National Academy of Sciences—National Research Council. The meeting was substantially supported by a grant from this Institute as well as by other Federal agencies, various foundations, the American Medical Association, and industry. Among those on the Executive Committee were Dr. W. Henry Sebrell, Jr., a former Director of the National Institutes of Health, and the Director, National Institute of Arthritis and Metabolic Diseases in his capacity as president of the American Institute of Nutrition. Staff members of this Institute participated actively in the program of this meeting which was most successful in providing those attending with stimulating ideas, challenging concepts, and worthwhile research findings.

Highlights of the Congress included a symposium on "World Food Needs and Food Resources" (opened by the Secretary of the Department of Health, Education, and Welfare), panels on the "Nutritional Status in Man," "Proteins and Amino Acids in Nutrition," "Lipids in Health and Disease," "Nutrition in Maternal and Infant Feeding," "The Effect of Processing and Additives on Foods," "Animal Nutrition and Food Production," and "New Possibilities in Nutrition Research." It was felt that this International Congress contributed substantially to an exchange of knowledge and cross-fertilization of scientific thought from diverse quarters, an essential to progress in this field of vast importance to human welfare.

CONCLUSION

The past year has witnessed important advances and solid research accomplishments in the various areas of responsibility of the Institute. Valuable improvements are steadily being achieved in the treatment of the diseases in which this Institute has special interests—the arthritides, diabetes, and endocrine, metabolic, gastrointestinal, and pediatric disorders. Simultaneously, by enriching our fund of basic biological knowledge we are broadening the foundation on which are based all future advances in the medical sciences and the art of healing. We hope that this balanced program of research for the development of fundamental new knowledge, and applied study to translate it into terms of practical benefit to the patients, will continue to be successful in the battle against disease and disability during the decades immediately ahead.

This year marks the 10th year of operation of the National Institute of Arthritis and Metabolic Diseases and we can reflect with pleasure on a decade of unparalleled progress in the treatment and prophylaxis of the diseases in the research province of the Institute. Much of this progress is due to the devoted, tireless work of the scientists in Bethesda and at research centers throughout the country who have toiled selflessly at the laboratory bench and the patient's bedside. But much is owed, as well, to the American people at large and their Representatives in Congress, who have had the understanding, willingness, and foresight to provide the wherewithall without which the most comprehensive research attack ever mounted against disease and disability, in which we find ourselves today, would not be possible.

On March 9 of this year, on the occasion of the spring meeting of the National Advisory Council of this Institute, we carried out a formal observance of this 10th anniversary. On that occasion leading legislators and scientists prominent in the fight against disease joined in a report to the Nation on "A Decade of Progress Against Arthritis and Metabolic Diseases." We wish to thank the members of this important committee, to which so much credit must go, for their able participation in this event.

In conclusion, Mr. Chairman, the amended request for 1962 is $68,740,000 as compared with the adjusted appropriation of $60,855,000 for 1961. This allowance for 1962 will provide for an estimated 370 additional research projects in arthritis, diabetes, gastroenterology, and various metabolic diseases. It further provides funds for direct research in the epidemiology and biometry program, for planned developments in the field of molecular biology and for general supporting services.

This request for 1962 is distributed among program activities as follows:

Grants:	
Research	$48, 530, 000
Fellowships	870, 000
Training	8, 300, 000
Direct research and supporting services	11, 040, 000
Total	68, 740, 000

TENTH ANNIVERSARY OF INSTITUTE

Dr. DAFT. The current fiscal year marks the 10th anniversary of the establishment of the National Institute of Arthritis and Metabolic Diseases.

Mr. FOGARTY. I am sorry we could not get out there that day, but that was a day we could not get away from here.

Dr. DAFT. We understood the situation. We were most sorry that you and Congressman Laird could not have been there. All of us missed you very much.

Last year before this committee I reviewed the remarkable growth of this Institute during its first 10 years and described to you a number of the important accomplishments of the period in our principal areas of special interest—arthritis, diabetes, and metabolism. I particularly emphasized the important role of the Congress, which by its steadfast support has made possible the sound development of our Institute's programs of research at Bethesda and of research and training grants.

On March 9 of this year a special program of observance of this 10th anniversary of the Institute was carried on. On this occasion outstanding public figures and leading scientists participated with us in a report to the Nation on a decade of progress against arthritis and metabolic diseases. In this year's statement has been described our current status after 10 years of vigorous growth. The statement also relates to you the Institute's most recent research and program developments.

RESEARCH ACCOMPLISHMENTS

I am happy to report several highly important research accomplishments, the significance of which lies primarily in the real progress which they signalize toward understanding of basic disease and life processes.

RHEUMATOID ARTHRITIS

In rheumatoid arthritis tremendous effort is being bent toward comprehension of the important immunological aspects of this disease. Perhaps one-third of all research in arthritis is being devoted to this approach. Increasing evidence is accumulating which suggests the possibility of an autoimmunity basis fo this form of rheumatic disease.

DIABETES

In diabetes a large-scale, carefully controlled study, coordinated at seven research centers, has been launched which will delineate with precision the natural history of the disease and may indicate the most effective means of preventing late complications. It is specifically designed to assess the long-term value of the oral drugs as compared with insulin. Other recent work on the oral drugs confirms and strengthens our belief in their long-term safety, although their effectiveness in a number of patients appears to disappear with time.

BIOCHEMICAL STUDIES

In fundamental biochemical studies two extremely important accomplishments, one at Bethesda, one at Pittsburgh, have opened up new avenues of approach which should have a far-reaching effect on our biological knowledge in the years to come. Institute investigators in Bethesda have demonstrated for the first time a concrete mechanism by which hormones exert their powerful controlling effect on biological processes.

SYNTHESIS OF ACTH

In the other important advance, grantee scientists at the University of Pittsburgh have just succeeded in putting together 23 amino acids to synthesize ACTH, the pituitary hormone which stimulates the adrenal cortex to produce cortisone and other essential hormones. This substantial advance was achieved by new techniques which will be applicable to the synthesis of a number of other hormones, even custom made or custom modified for specific desirable effects, and should open up for our understanding many aspects of endocrinology and metabolism. These are but the high spots in the tenth year of life of this Institute.

I should be happy to elaborate on any of these points.

Mr. Fogarty. I wish you would. I think I get as many questions asked of me during the year about what progress is being made in arthritis as I do in heart, cancer, and mental health.

Dr. Daft. It might be of some interest to you, Mr. Fogarty, to try to summarize some of the things that were said at our 10th anniversary.

Mr. Fogarty. All right.

Dr. Daft. This shows the advances during the past year.

We had at the 10th anniversary program five scientific speakers. For arthritis there was Dr. McEwen. For diabetes and endocrine diseases was Dr. George Thorn. For gastroenterology was Franz Ingelfinger. For metabolic diseases was Dr. DeWitt Stetten, Associate Director of our Institute. For metabolism and enzymology was Dr. Arthur Kornberg, Nobel Laureate and former Chief of our Laboratory of Biochemistry and Metabolism.

ARTHRITIS

I might start with the arthritis part of it. In the field of the rheumatic diseases Dr. McEwen stressed two particular developments as being outstanding in the past year particularly. The first, which was mentioned also by Dr. Lamont-Havers of the Arthritis and

Rheumatism Foundation, is a cooperative long-range study of the best treatment for rheumatoid arthritis. This study is sponsored by the American Rheumatism Association, the Arthritis and Rheumatism Foundation, and the NIAMD.

In selected clinics throughout the United States physicians are cooperatively testing the newer drugs on adequate numbers of patients. This serves a dual purpose, one to give authoritative information to all physicians on the best forms of treatment of arthritis and, second, to speed up greatly the clinical application of laboratory findings. This is the first time that there has been prompt testing of the newer drugs on an adequate number of patients. Frequently over the course of a few years after drugs have been introduced there has been sporadic testing with results which at times has been misleading to physicians, but never has it been completely adequate. This cooperative long-range study is just beginning, has tested a few drugs at the present time, but will serve, we think over the years ahead, to give prompt information to all physicians on the best form of treatment of arthritis.

The second point stressed by Dr. McEwen concerns the very encouraging studies on the cause of the rheumatic diseases. It is becoming increasingly certain that certain members of this group of diseases are caused by or related to hypersensitivity.

I might interrupt to say this has been known for a long time in relation to rheumatic fever. It is quite clear that in this disease there is hypersensitivity, in this case to certain bacteria.

In the case of two of the other diseases of this group, however, it seems to be a case of autoimmunity. These diseases, closely related to rheumatoid arthritis, are lupus erythematosis and what is called Sjogren's Syndrome. The latter one is characterized by some of the same things which you find in the autoimmunity to protein of the thyroid gland, mentioned in the report by the Allergy Institute.

However, it also has many aspects in common with rheumatic diseases. A certain percentage of patients also have arthritis, and almost all of them show the same material in the blood, which is found in patients with rheumatoid arthritis.

It has become evident, therefore, that in these diseases, and possibly in rheumatoid arthritis as well, there may be derangement of immunological mechanisms involving autoimmunization.

In the words of Dr. McEwen, and I quote,

> This theory has not yet been proven but there is much evidence which supports it. At the moment there is reason to hope that we may be getting closer to the breakthrough which has been so long sought.

I think those were the principal things in the field of rheumatoid arthritis that were reported at this meeting.

OSTEOARTHRITIS

Mr. Fogarty. What is the form of arthritis that often affects the hips?

Dr. Daft. The two very serious forms are rheumatoid arthritis and osteoarthritis.

Mr. Fogarty. Osteoarthritis is what I was thinking of.

Dr. Daft. That is frequently found in the hips.

Mr. Fogarty. I know two or three Members of Congress who are suffering from it quite a bit. Have you made any progress in that field?

Dr. Daft. We have made some. I am sorry to say that there has been nothing dramatic in the past year or, for that matter, at any time in the treatment of osteoarthritis. The things that can be done are to make the patient more comfortable, to prevent crippling from the disease to a very large extent, but as for a cure of the disease——

Mr. Fogarty. What do you do to make them more comfortable and prevent crippling? Is it exercise?

Dr. Daft. Exercise will help in preventing crippling. The best treatment remains aspirin. That is palliative, very largely.

There are a number of studies going on trying to learn more about the disease, and we are learning more about the disease, progress is being made every year. But in the field of treatment I am sorry to say there is nothing very dramatic over the past several years.

Mr. Fogarty. Are you concentrating on it as much as you think you should? Are you spending as much effort in that field as you are on rheumatoid arthritis?

Dr. Daft. Probably not.

Mr. Fogarty. There are not so many people involved, are there?

Dr. Daft. No, it is not as serious a disease in the sense of permanent crippling. It is an extremely uncomfortable disease, and I know that people who have osteoarthritis would probably not agree that it is a less serious form of disease than rheumatoid; yet, speaking objectively, it probably must be considered a somewhat less serious form of the disease. Rheumatoid arthritis is called the great crippler and is certainly the more serious form of the two.

There is considerable effort being spent on it, not as much as on rheumatoid arthritis, I think, for two reasons. One is that when there is a lead, as there is in rheumatoid arthritis, a hope that we are finding the cause, people get very interested in that and spend more effort in it so that a great many more people are interested today in rheumatoid arthritis than are interested in osteoarthritis.

There are a number of investigators working along quietly and hopefully. One of these days one of them will develop a lead, and in that case I am certain we will get a great deal more interest in it.

Mr. Fogarty. Go ahead.

ROLE OF DNA IN HEREDITY

Dr. Daft. In some of the other fields, which are a little more difficult to explain, I might report to you just a little bit on Dr. Kornberg's presentation.

Mr. Fogarty. Tell us a little about each.

Dr. Daft. Very well.

Starting at this time with Dr. Kornberg's, which is rather basic to the presentation by Dr. Stetten, Dr. Kornberg's remarks revolved around the transmission of biochemical and genetic information. He compared this transmission of information to the recent case we read about in the paper where information was being sent by means of microdots.

Mr. Fogarty. By what?

Dr. Daft. By very small dots about the size of a regular period on a piece of paper, and each one of those, when studied under a very strong microscope, revealed a complete message. This was mentioned in a recent spy case in the newspapers. This was certainly a very ingenious method of transmitting information, but compared to the type of transmission of information Dr. Kornberg was talking about, it is very crude and is really not a micro method at all because he is talking about transmission by chemical molecules.

One of the most exciting basic advances in the past couple of years in this country, the past several years, has been the identification of one substance in cells as being the transmitter of hereditary information. That substance is called DNA—deoxyribonucleic acid. This material in the fertilized egg is the material which determines whether the egg will develop into a rooster, a hen, a cow, an elephant, or nothing at all. In Dr. Kornberg's words:

> It is in crude analogy the book of life, and like some useful books, it contains the instruction for building something—in this case the intricate structure and enzymatic machinery of the cell, the enzymes, proteins, and all other parts of this complex chemical fabric. This is one function of DNA. The other and equally important function is that it provides for the preservation of the race. Having taken care of the development of the cell, it also, like a book, can be copied or reproduced so exactly that an identical cell will develop, and so on ad infinitum

DNA—deoxyribonucleic acid—is a very large molecule made up of just four building blocks. So for this alphabet we have only four letters. Each one of these molecules of DNA, however, is thousands of building blocks long, so that the variations in the use of these letters can transmit very complicated messages, as we have seen, because it transmits the complete message of whether this cell is to develop into an animal or whatever it should develop into.

If one of the letters in this long DNA message is altered by radiation or by other means or an error is made in copying, then the resulting mistakes in the activities of the new cells may be costly or even fatal. If the changes are great, loss of life results. If the changes are relatively small, in the case of humans, an individual with an inborn error of metabolism, a metabolic disease, if you like, develops.

GENETIC ABNORMALITIES

This brings me to Dr. Stetten's portion of the talk. Dr. Stetten showed us a book of some 200 pages published in 1908.

Mr. Fogarty. Who is Dr. Stetten?

Dr. Daft. Dr. Stetten is the Associate Director, the Scientific Director of the Arthritis Institute. He has given scientific leadership to our Institute over the past 5 or 6 years. He is a very distinguished investigator in his own right, as well as now a research administrator. He showed us first this book published in 1908, a volume of 200 pages or so, the collected lectures of Sir Archibald Garrod, which was called "Inborn Errors of Metabolism."

It was noted that all of these diseases are familial, all six of them he discussed, all are characterized by rather bizarre abnormalities, which could be defined chemically. Dr. Stetten then showed us another book, a volume of some 1,500 pages, a much larger volume, published a few months ago. It is entitled "The Metabolic Basis of Inherited Disease," by Stanbury, Wyngaarden, and Frederickson. Dr. Wyngaarden, I might add, is an alumnus of our Institute, NIAMD, and is now at Duke University. Dr. Frederickson is a member of the staff of the Heart Institute and has recently, I believe, been made Clinical Director.

The subject matter of this new book is basically the same as the one published in 1908, but now in excess of 50 diseases had to be treated, these at a very much different level of sophistication. They were treated in a way that the author, of course, in 1908 would not have understood. The specific chemical defects in these metabolic diseases are in many cases known today. In sickle-celled anemia, for example, the defect in the DNA which Dr. Kornberg spoke about, of the parents of the individuals with the disease, has been transmitted to the child and has resulted in a hemoglobin molecule which, curiously enough, differs by only one amino acid out of a very large number from normal hemoglobin.

Despite the fact that this seems a very small difference between sickle-celled hemoglobin and normal hemoglobin, this very small change results in a very serious disease.

In galactosemia, which has been discussed before this committee in previous years, the defect—again in the DNA discussed by Dr. Kornberg—has resulted in one very important protein, in this case an enzyme, being completely absent. The missing enzyme in this disease is needed for the proper utilization of milk, more specifically, for the transformation of the sugar in milk to glucose. As a result, if the infant with galactosemia is given milk, a chemical compound resulting from the partial transformation of the milk sugar, called galactose-1-phosphate, accumulates in the body. This material which accumulates is injurious to the liver, brain, the lens of the eye, and possibly other tissues. If milk is not promptly removed from the diet the infant dies or if he lives becomes blind and mentally defective.

It is, I am sure, quite apparent from this discussion that these so-called metabolic or inherited diseases are of very great interest to more than one Institute in Bethesda. There is fine cooperation between the investigators in the various institutes in these areas. We feel very excellent progress is being made in this group of diseases.

As pointed out by Dr. Stetten—

> Most of the growth in knowledge in this area has taken place in the last decade and most of it has resulted from the fusion of techniques and of thinking of enzymologists, geneticists, physical chemists, and physicians. We believe that it is no accident that 2 of the 3 editors of this large volume, and no less than 15 of its contributing authors, either have served or are now serving sizable portions of their professional careers at the National Institutes of Health. The opportunities for such collaborative assault upon disease are, we believe, unmatched anywhere in the world.

If I may, I should like to add that for this fact we are certainly indebted very much to this committee for their far-seeing statesmanship over the years in supplying us the clinical center and other facilities to make this possible.

This covers three of the areas.

I might mention very briefly some points given by the other two.

DIABETES

Dr. George Thorn, in reporting on diabetes, mentioned the cooperative study now underway on the long-term clinical evaluation of the oral drugs and spoke also of the recent studies indicating that these compounds act by stimulating insulin secretion as well as by decreasing glucose production by the liver. It was once feared that the stimulation of the pancreas to secrete insulin, particularly in mild diabetics, might lead to exhaustion of the pancreas and thus result in a more severe form of the disease.

It is most heartening that studies on the rat, the dog, and on man, some of them completed within the past year, indicate that these fears were unfounded. It remains to discover the effects of the oral drugs, as compared to insulin or to special diets alone, in preventing the late complications of diabetes. Studies along this line are in progress.

GASTROENTEROLOGICAL DISEASES

Dr. Ingelfinger, reporting on the field of gastroenterology, emphaphasized advances in the treatment of children and adults with celiac disease and sprue.

Mr. Fogarty. What is that?

Dr. Daft. Celiac disease is characterized by a very severe GI upset, wasting away due to lack of ability to get nourishment from food. In many cases this has resulted in death. Sprue is a disease of adults. There is tropical sprue and nontropical sprue. A great many cases are found in the tropical regions.

There are also a few cases in this country, however. Again it is characterized by a very typical form of diarrhea, which is almost diagnostic of the disease.

It has been found first in Holland and later in other countries that this can be treated by the removal of an offending food from the diet. It is a portion of wheat flour. These patients have been treated quite successfully by giving them diets which do not contain gluten, which is the offending thing in the diet.

Another advance mentioned by Dr. Ingelfinger was the treatment of patients with advanced liver disease with diet and antibiotics.

He stressed also advances in our understanding of cystic fibrosis.

Mr. Fogarty. Does alcoholism have anything to do with liver disease?

Dr. Daft. Yes, sir. He spoke in particular of liver cirrhosis. In liver cirrhosis very frequently there is an inability to take care of certain of the products of digestion and to a certain extent products of bacterial action on food materials—which causes the production of ammonia. Instead of the ammonia being turned over to urea, it remains as ammonia and it may lead to coma and death from the disease.

There has been a great deal of advance in our understanding of this problem, and by careful treatment of the patients with diet, and particularly by antibiotics, we can prevent some of the bacterial action on food products.

They have been able to limit ammonia production to a very considerable extent.

Mr. Fogarty. Proceed.

CYSTIC FIBROSIS

Dr. Daft. I was going to mention that in the area of cystic fibrosis our research program at Bethesda has been underway about a year and is making good progress.

I think Dr. Andrews has submitted for the record our report to the committee on the work, not only at Bethesda but throughout the United States, by the two Institutes in the area of cystic fibrosis.

That is all I have, Mr. Chairman.

REQUESTED 1962 BUDGET

Mr. Fogarty. Your 1961 appropriation after adjustment for transfers is $60,855,000, and the 1962 Eisenhower budget is $62,239,000, or a net increase of $1,384,000. The budget amendment adds $6,501,000 making a total net increase of $7,885,000.

Will you give us the history of your regular 1962 request and the history of the budget amendment?

Dr. Daft. Yes, sir.

(The information requested follows:)

Development of 1962 budget estimates for arthritis and metabolic disease activities

[In thousands]

Obligations by activity	Original Institute estimate to National Institutes of Health	Reduction by National Institutes of Health	Preliminary estimate to Public Health Service	Reduction by Public Health Service	Department of Health, Education, and Welfare to Bureau of the Budget	Reduction by Bureau of the Budget	1962 original estimate	Department of Health, Education, and Welfare revise submission to Bureau of the Budget	Reduction by Bureau of the Budget	1962 revised estimate
Grants:										
Research	$57, 520	−$5, 490	$52, 030	−$1, 635	$50, 395	−$7, 970	$42, 425	$53, 027	$4, 497	$48, 530
Fellowships	2, 500	−1, 330	1, 170	0	1, 170	−300	870	1, 170	300	870
Training	14, 060	−5, 760	8, 300	0	8, 300	0	8, 300	8, 300	0	8, 300
State control programs	0	0	0	0	0	0	0	0	0	0
Community demonstration projects	0	0	0	0	0	0	0	0	0	0
Total grants	74, 080	−12, 580	61, 500	−1, 635	59, 865	−8, 270	51, 595	62, 497	4, 797	57, 700
Direct operations:										
Research	10, 487	−623	9, 864	−114	9, 750	−285	9, 465	9, 725	0	9, 725
Biologics standards	0	0	0	0	0	0	0	0	0	0
Review and approval	1, 029	−97	932	+13	945	−15	930	1, 174	124	1, 050
Training activities	0	0	0	0	0	0	0	0	0	0
Professional and technical assistance	0	0	0	0	0	0	0	0	0	0
Chemotherapy contracts	0	0	0	0	0	0	0	0	0	0
Administration	354	−102	252	0	252	−3	249	265	0	265
Total direct operations	11, 870	−822	11, 048	−101	10, 947	−303	10, 644	11, 164	124	11, 040
Total obligations	85, 950	−13, 402	72, 548	−1, 736	70, 812	−8, 573	62, 239	73, 661	4, 921	68, 740

Mr. Fogarty. What did you originally request?

Dr. Daft. The original estimate to NIH was $85,950,000.

Mr. Fogarty. As compared to what?

Dr. Daft. $68,740,000.

Mr. Fogarty. They gave you a good cut; didn't they? Do you still think you can effectively use $85 million if you had it?

Dr. Daft. The present budget, sir, will permit some increases, particularly in research grants.

Mr. Fogarty. Dr. Shannon, is this something every Institute Director is told to say when asked that question?

Dr. Shannon. No, sir.

Mr. Fogarty. They all give the same answer. It seems to me that they must have received some orders from you, the Secretary, the Surgeon General, Mr. Kelly, or someone.

Dr. Shannon. They were asked to make a realistic appraisal. They were not instructed to say they could not use additional amounts nor were they instructed to indicate how much they could use, Mr. Fogarty.

Mr. Fogarty. I asked if he could still use the $85 million. You will get around to answering that; won't you, Doctor?

Dr. Daft. I am sorry; I paused for breath there. I was going to say "Yes, sir."

Mr. Fogarty. It seems to me everybody has the same stock answer about the progress that the budget will permit and strain to get it in some way even if they have to make an unresponsive answer to some question we ask.

Do you think you can effectively use any more than $85 million? Suppose we gave you $95 million? Supply for the record how you would use that amount.

Dr. Daft. Very well, sir.

(The information requested follows:)

Breakdown of budget of $95,000,000 as requested

Activities	
Grants:	
Research	[1] $63, 900, 000
Fellowships	2, 500, 000
Training	[2] 16, 000, 000
Total grants	82, 400, 000
Direct operations:	
Research	10, 868, 000
Review and approval of grants	1, 407, 000
Administration	325, 000
Total direct operations	12, 600, 000
Total	95, 000, 000

[1] Including $1,500,000 for additional foreign grants.
[2] Including $2,000,000 for experimental training grants in Departments of Medicine.

Research projects, increase $15,370,000 over 1962 amended budget

The research grants program of the Institute is the backbone of its extramural activities and the essential foundation on which a major share of the progress in biomedical research in the fields of responsibility of NIAMD is based. In terms of money, the research grant program is the most important single component of the Institute's extramural budget.

The requested estimate of increases would permit a positive response to requests for support of proposed investigations of high quality and for exploitation of the opportunities resulting from the entrance of new qualified investigators into the field of research responsibility of the Institute. It is felt that the proposed budget would achieve the twin objectives of pursuing promising and productive research leads while simultaneously permitting the initiation of additional projects with productive potential.

An item of $1,500,000 is included to extend support of investigators outside the United States in areas of special interest to this Institute, where the research can be better done outside the limits of this country or where the research results would be of great benefit to our citizens.

Fellowships, increase $1,630,000 over 1962 amended budget

Additional funds in the fellowships area would support a growing interest in training for basic research and clinical investigation in problems relating to arthritis, diabetes, gastroenterology, and general metabolism. During fiscal years 1960 and 1961 there has been a significant increase in numbers of applications in those fields.

Training—Increase $7,700,000 over 1962 amended budget

Additional funds for graduate training grants would support training of manpower for development of program for academic medicine, including clinical research, in medical schools currently not engaged in or not adequately staffed for these purposes. Such programs in this estimate include not only the traditional five major areas of support (arthritis, diabetes, gastroenterology, hematology, and general metabolism), but also provide for support in the new areas of dermatology, orthopedics, and nutrition.

DIRECT OPERATIONS

Research—Increase $1,143,000 over 1962 amended budget

Included in this activity—in addition to fundamental laboratory studies and an extensive clinical investigations program—are international studies in civilian nutrition conducted throughout the world in collaboration with the Interdepartmental Committee on Nutrition for National Defense, and collaborative epidemiologic, biomathematical and genetic programs conducted by the Institute's Epidemiology and Biometry Branch. The following brief explanation indicates the areas in which additional funds would be used: $150,000 to support expanded programs in international civilian nutrition studies in selected countries throughout the world; 3 positions and $150,000 to strengthen the epidemiology and biometry staff and provide funds for contracts with cooperating universities in the United States and abroad and for mobile epidemiologic field studies, including the purchase of a mobile van or trailer; 22 positions and $417,000 for additional staff and equipment to support studies conducted by senior investigators in the field of molecular biology, nutrition research, enzymes, and cellular biochemistry, physical biochemistry, physiology, metabolic enzymes, clinical hematology, gastroenterology, and clinical diabetes studies. The total also includes funds to purchase computer time for research in computer technology as applied to biology and for the purchase of specialized items of equipment and the replacement of obsolete scientific equipment. Included, also, is $426,000 for research services furnished centrally.

Review and approval—Increase $357,000 over 1962 amended budget

$158,000 and 12 additional professional and clerical personnel are provided to administer the proposed expanded grants programs. This includes funds for initial equipment requirements, travel, printing and publication, communications, and other miscellaneous expenses. Further provided is $199,000 for services furnished centrally.

Administration—Increase $60,000 over 1962 amended budget

The increase provided for this activity is for three positions and $31,000 to furnish staff assistants to the Institute Director for special program analysis and review activities and for the planning and preparation of a projected series of special and continuing reports covering all Institute programs. Also included is $29,000 for services furnished centrally.

BACKLOG OF APPROVED GRANT APPLICATIONS

Mr. Fogarty. What will be the total of approved but unfinanced grant applications at the end of 1961?

Dr. Shannon. There will be no deficit if there are no institutional research grants at the same time.

Mr. Fogarty. What is the story for 1962?

Dr. Shannon. If this budget is approved, the deficit with the institutional research grants will be $6,490,000. If institutional research grants are not approved for the coming fiscal year, it will be $4,134,000.

ORAL DRUGS FOR DIABETES

Mr. Fogarty. Have there been any recent advances in oral drugs for diabetes? How widely are they used?

Dr. Daft. I would say about the same percentage of people use them. It is estimated around 35 or 40 percent of all diabetics are on oral drugs. There have been a few patients, just the number I cannot say, who after some time have no longer been benefited by the oral drugs, so those have dropped out of the list that are successfully taking them.

On the other hand, it has been found that a combination of oral drugs, or combinations of oral drugs with very small doses of insulin, have worked in many cases, so that in the former case, when combinations of two types of oral drugs are now working, this would be an increased number of patients who can successfully take them.

I believe on balance it is probably about the same number, some 35 or 40 percent who are no longer taking injections of insulin.

GASTROENTEROLOGY

Mr. Fogarty. In the field of gastroenterology, are we doing as much there as we should?

Dr. Daft. With your help there has been a tremendous advance. One thing that Dr. Ingelfinger pointed out was the status of gastroenterology just a few years ago and where it is today, and the improvement in the status of the field, improvement in the amount of research going on in the field. It has been dramatic.

Some 5 years ago, at the most 8 years ago, we were supporting a mere handful of research grants in gastroenterology. At the present time we are supporting more than 300.

A few years ago there were practically no departments of gastroenterology—a very few in the country.

As Dr. Ingelfinger pointed out much better than I could, it was a field not in ill repute but at least it did not have the status which a field of its importance should have had.

Today there are 41 training grants in the field of gastroenterology supported by the Institute. It is being incorporated into the Department of Medicine in the form it should be. I think all of the gastroenterologists feel there should not be separate departments, that this would fragment medicine, that it should remain as part of the general field of medicine, and our training grants should, as they are doing, stress research training, which is very badly needed in this field.

I think we can always do more. There are many more things to be done in the field of gastroenterology, but I think what has been accomplished over the last few years has really been tremendous.

HEPATITIS

Mr. Fogarty. What about hepatitis?

Dr. Daft. Hepatitis probably would be covered very largely under another Institute because it is an infectious disease. Hepatitis is caused by a virus, two different viruses.

Mr. Fogarty. Page 13 of the justifications mentions you are giving some support to hepatitis research.

Dr. Daft. Undoubtedly, the metabolic aspects. For a moment that slipped my mind. We have been giving support to some of the metabolic abnormalities resulting in cases of hepatitis.

CHILD HEALTH CENTER

Mr. Fogarty. What are you doing in pediatrics?

Dr. Daft. We are supporting a number of areas of pediatrics. As you know, there is now a child health center at the Institute which cuts across Institute lines and does not change in any degree our support of it at the present time.

Mr. Fogarty. Is that child health center in operation?

Dr. Daft. As an intelligence function. It is my impression it is operating very well. I would have to defer to Dr. Shannon on that.

Dr. Shannon. No. As we brought out, this is now being carried as a staff function. Dr. Stone, Assistant Chief, Division of General Medical Sciences, is carrying this out using the staff of this Division and my own office as a means of gathering information on what is underway now in the various Institutes and formulating plans on how this area could be stimulated should this direction be given to it.

I think a great deal of the work that would relate to child development is being carried in the Division of General Medical Sciences now.

I think Dr. Daft's primary interest is specifically in certain of the diseases that are more common in children or more easily studied in children rather than in the child's development.

Mr. Fogarty. Is it your intention to go ahead and set up this Child Health Center?

Dr. Shannon. This is our purpose.

Mr. Fogarty. Suppose we say in the report we think you ought to carry on this function as is? What will you do then?

Dr. Shannon. We still would carry on the function. This is work we will do in any case as part of our normal program development.

If so directed we would not follow formal representation within the hierarchy of our Institute's structure.

I say this because we have been doing a great deal of work and study in the field of child development over the past 2 or 3 years. To say "stop" would mean to backtrack on many programs firmly established.

Mr. Fogarty. I am sure we won't recommend any backtracking in research in this field. We might make suggestions that you spend twice what you are spending. But I think there is some disagreement among professional people in this field as to the best way of organizing this program.

DERMATOLOGY

What are you doing in dermatology?

Dr. Daft. We have a number of training grants in the area of dermatology. Dermatology, as gastroenterology, has been, from a research point of view, very greatly neglected. We are trying very hard to do something about it.

I think we have something like 20 training grants in the area of dermatology at the present time. We are setting up a training grant committee because of the number of requests we are getting in this area. These are for research training, and we hope this will have the same impact on this field as our programs have had in the field of gastroenterology.

Mr. Fogarty. It is often a pretty serious disease, is it not?

Dr. Daft. Yes, sir.

Mr. Fogarty. It affects many people?

Dr. Daft. There are very many serious diseases included in this general area of dermatology. It is a group of diseases rather than a single disease.

In the Cancer Institute they cover all cancers of the skin, which would be in their particular area.

ORTHOPEDICS

Mr. Fogarty. What are you doing in orthopedics?

Dr. Daft. In orthopedics we are supporting some research and training. It is relatively small at the present time. Orthopedics is an area of considerable interest to all rheumatologists because of the fact that in both osteoarthritis and rheum-arthritis it becomes one area of therapy under certain conditions.

GEOGRAPHIC STUDIES

Mr. Fogarty. What are you doing in the field of geographic studies?

Dr. Daft. We have a new branch of epidemiology and biometrics, and in that branch, one section is carrying on studies in geographic diseases. This is true in a number of what we believe to be important and interesting areas.

There are biochemical differences between population groups which are undoubtedly related to disease. There are some very important disease differences between population groups among the chronic diseases.

In Japan they see practically no diabetes, so we are told. This appears to be true in some other areas of the world.

We have been making some studies of the disease distribution of arthritis and some of the related diseases in this country in the hope this will give us a clue as to what might be causing the disease in these population groups, so we are carrying on a number of studies in this general area, some of them in the United States and some of them outside the United States.

One I might mention specifically, where we are just making a beginning, there is a very curious taste difference, ability to taste certain substances in the population in this country as well as the population in other countries. This test has been used very interestingly in a lecture by Dr. Beadle, which he gave at NIH several years ago.

About 1 in 5 can taste this particular compound. The other four people do not taste it at all.

He passes out paper impregnated with this compound in the audience and 1 person in 5 tastes it. It is a very unpleasant taste to him. The other four-fifths of the people do not taste it at all.

This compound is related chemically to some compounds which cause goiter, so there is just a possibility that the people who cannot taste this type of compound are those who will eat materials which will cause goiter. This study is in its first stages at the present time.

CAREER PROFESSORSHIPS

Mr. Fogarty. I notice you are budgeting for 15 career professorships for 1961–62.

Dr. Daft. Yes, sir.

Mr. Fogarty. Does this mean you will be financing 30 in 1962 or will you continue the 15 granted in 1961?

Dr. Daft. We would continue 15.

Mr. Fogarty. In the justifications you say these are meant to serve as a stabilizing support of outstanding and distinguished academic careers. What do you mean by that?

Dr. Daft. As the research in this country has grown there have not been a sufficient number of so-called tenure positions in the universities, and it has become a problem, therefore, how to give stable careers to people very thoroughly deserving and at an age where they should have a professorship and would have a professorship on the basis of their attainments were it not for the fact there are just not enough professorships available.

Mr. Fogarty. How much is the average pay of these professors?

Dr. Shannon. Calculated at a $20,000 average, with an upper limit of $25,000.

Mr. Fogarty. Does the salary come entirely from the Federal grant?

Dr. Shannon. In this case it would, yes.

Mr. Fogarty. Is there anything else you want to say, Doctor?

Dr. Daft. No, sir.

Mr. Fogarty. Dr. Shannon?

Dr. Shannon. No, sir.

Mr. Fogarty. Thank you very much.

Incidence and Cost of Arthritis and Metabolic Diseases

We shall place your statements on the incidence and cost of these diseases and your statement on the highlights of research in the record at this point.

(The statements referred to follow:)

ARTHRITIS AND METABOLIC DISEASE ACTIVITIES

Statistics concerning the annual number of deaths and total current number of disabilities caused by some of the major diseases under study in the National Institute of Arthritis and Metabolic Diseases and the estimated annual cost to the Nation:

I. Deaths during 1959 (National Office of Vital Statistics):

Category:	
Diabetes mellitus	28,080
Gastrointestinal diseases (ulcer of stomach and duodenum, and cirrhosis of the liver)	29,916
Total	57,996

II. Disabilities (National Health Education Committee, Inc., 1960):

Rheumatic diseases (600,000 persons completely disabled and 2,200,000 persons partially disabled)	2,800,000

III. Estimated annual economic cost to the Nation (National Health Education Committee, Inc., 1960):

Rheumatic diseases (arthritis, rheumatism, gout)	$1,000,000,000

(There are an estimated equivalent of 68,000 full-time wage earners constantly out of work due to arthritis and rheumatism.)

HIGHLIGHTS OF PROGRESS IN RESEARCH ON ARTHRITIS AND METABOLIC DISEASES, 1960

Items of interest on program developments and research studies conducted and supported by the National Institute of Arthritis and Metabolic Diseases

The scientific advances described on the following pages are categorized under various disease headings, but this has been done mainly for the convenience of the reader and not because of any real separation between the fields as far as fundamental knowledge is concerned. As research progress continues, it becomes increasingly apparent that underlying all the fields is a substructure of basic research knowledge common to all the medical sciences. Obtaining this basic knowledge is one of the primary activities of the National Institute of Arthritis and Metabolic Diseases.

Many times the results of basic studies have no direct application to treatment, such as the major finding made this year about the manner in which hormones directly affect key metabolic processes within a cell. Although this discovery has no immediate clinical use its implications are obvious since hormonal activity is involved in many diseases. Occasionally, however, basic studies lead directly to dramatic developments. Basic laboratory studies on burn shock at the Institute have now culminated in an effective gamma globulin treatment for severe post-burn infections that are otherwise fatal.

In addition to its original areas of interest—rheumatic diseases, metabolic disorders, gastroenterology, hematology and nutrition—the Institute has recently acquired three new fields of responsibility, pediatrics, orthopedic surgery, and dermatology. The diversity of these fields makes it even more necessary to strengthen basic research. Today, Institute scientists and grantees are focusing their attention on the root causes of disease. Mere palliation is no longer enough, for no matter how effective symptomatic relief becomes it cannot prevent disease. It is this prevention, not treatment, that is the ultimate goal of medical research.

RHEUMATIC DISEASES

During the past 10 years, under the auspices of the Institute, a tremendous increase has occurred in research on arthritis and the other rheumatic diseases, and great improvements have been made in the treatment of these disorders. Since cortisone was first used in 1948, the pharmaceutical industry has developed a whole spectrum of corticosteriod drugs, many of which have been tested at the Institute, for the relief of pain and inflammation. Thousands of arthritics have benefited from these successors to cortisone, but unfortunately the drugs cannot cure the underlying disease. Thus, research must continue to be directed toward basic causes. Recent studies have added further support to the concept that several of the rheumatic diseases result from a State of hypersensitivity, and may be diseases of autosensitivity in which a person becomes overly sensitive to substances that are normally present within his body.

Study shows that arthritis is more widespread than believed

Evidence that rheumatoid arthritis may be at least 6 times more widespread than has been generally assumed was reported to the annual meeting of the American Rheumatism Association by grantees of the National Institute of Arthritis and Metabolic Diseases. A survey of employed workers at the Oak Ridge (Tenn.) National Laboratory indicates that many cases of rheumatoid arthritis may go undiagnosed because the disease runs a benign, remittent course with mild-to-moderate symptoms and little disability.

In the past, the best available estimates put the number of arthritis sufferers at about 2½ percent of the total population of the United States. The present study of 331 craftsmen and their foremen shows that mild rheumatoid arthritis affects about 15 percent of regularly employed plantworkers. Usually, the course of the disease was mild to moderate and disability was rare.

The study was begun after it was found that one out of four employees came to the Oak Ridge National Laboratory's dispensaries because of a rheumatic complaint. The survey was conducted over a 28-month period and included medical screenings of the workers which were done monthly for the first 16 months and quarterly thereafter. A carefully trained nurse was instructed to ask pertinent questions and to make brief joint examinations, and men with swollen joints were immediately referred to the plant physician for examination. Uniform diagnostic criteria, established by the American Rheumatism Association, were used throughout the study, and included morning stiffness. pain on motion or tenderness, observed swelling, swelling of two or more joints and symmetrical swelling.

The NIAMD grantees, Drs. Thomas A. Lincoln, Medical Director, Oak Ridge National Laboratory, and Sydney Cobb, University of Pittsburgh, reported that by the end of the study 5 percent of the screened employees had been diagnosed for "definite" rheumatoid arthritis and an additional 10 percent for "probable" rheumatoid arthritis—making a total of 15 percent who at some time during the 28-month study were classified for "probable" or "definite" rheumatoid arthritis.

Increased frequency of rheumatoid arthritis with age has also been observed. Of 93 men between 50 and 66 years of age, 10 percent had "definite" and an an additional 12 percent had "probable" rheumatoid arthritis.

The investigators pointed out that the final percentage of men affected by rheumatoid arthritis would probably have been higher if medical observations had extended beyond the 28-month period. This is also borne out by the fact that during the study's first month only 2 percent met the criteria for probable or definite rheumatoid arthritis. As observations continued, increasing numbers of employees were admitted to these two diagnostic criteria. It was apparent that a prolonged period of observation was necessary to properly classify theses patients since most of them were free of joint swelling most of the time.

Standard latex agglutination tests were also done on sera from the patients. Though the tests were negative in most of these cases of mild arthritis, the patients had significantly more latex agglutinating substance in their sera than do normal individuals, but had less than clinical cases of rheumatoid arthritis.

It thus appears that rheumatoid arthritis may be a disease that is much more common (and benign) than has been supposed, the NIAMD-supported investigators reported, and they concluded from their study that rheumatoid arthritis affects a substantial portion of a group of regularly employed men. In contrast to the more severe cases usually seen in clinics and consulting rooms, these cases seem to run a benign remittent course with mild to moderate symptoms and little disability.

Discover new side effect of corticosteroid drugs

Clinical investigators at the National Institute of Arthritis and Metabolic Diseases in collarobation with the National Institute of Neurological Diseases and Blindness have discovered a heretofore unnoticed side effect of corticosteroid therapy—the production of slight opacities in the lens of the eye. These opacities (posterior subcapsular cataracts) in most cases cause no impairment of vision and do not require surgery. They are distinct from the more serious "senile" type of cataracts which result in failing vision and require surgcal removal of the lens.

The lens opacities were first noticed in four rheumatoid arthritis patients at the Institute who were receiving prolonged therapy with synthetic corticosteroids. The eye lesions consisted of small filament-like spots present on the posterior surface of the lens and occurred in both eyes. Such cataracts are generally associated with exposure to toxic agents, eye disease or injury, or exposure to radiation, but since none of these factors were implicated in the four cases, the NIAMD and NINDB investigators began a careful examination of 66 rheumatoid arthritis patients available for study at the Institute. Of this group, 44 had received steroid therapy while 19, who served as the control group, had not.

The investigators, Drs. Roger L. Black, Richard B. Oglesby, Ludwig von Sallman and Joseph J. Bunim, found the posterior subcapsular cataracts in 17 of the 44 steroid-treated patients (39 percent) and none in the non-steroid-treated control group. The appearance of these opacities was uniform and easily distinguished from the more common cataracts. In 11 of the 17 cases the opacities were visible with an ophthalmoscope. Only 6 of these 17 patients had experienced any symptoms from the opacities and in only 4 of these 6 was there any measurable loss of vision. The visual loss was slight (a change from 20/20 to 20/40 vision), and no case required surgery.

There was a striking relationship between the amount of corticosteroid received and the occurrence of the lens' opacities. For purposes of the study the steroid-treated patients were divided into three groups: a "low dosage" group who had received on the average less than 10 milligrams daily of prednisone or its equivalent; a "midrange dosage" group receiving 10 to 15 milligrams daily; and a "high dosage" group receiving 16 milligrams or more per day. No patients in the low dosage group had developed opacities whereas 23 percent of the midrange dosage group and 75 percent of the high dosage group had developed the eye lesions. The duration of the corticosteroid therapy was also significant in the production of the opacities but to a lesser extent than the dosage level.

The relatively young age of the patients developing the opacities (10 of the 17 were less than 50 years of age) further supports the evidence that the posterior subcapsular cataracts were not of the senile type. Additionally, of all the patients over 50 in the study, none of the nonsteroid-treated ones were found to have posterior subcapsular cataracts whereas half of the steroid-treated patients in this age group developed the condition.

No specific corticosteroid preparations were implicated; there was no apparent difference between the various drugs used (cortisone, hydrocortisone, prednisone, triamcinalone, 6-methyl prednisolone and dexamethasone) as far as their likelihood of producing the opacities. The mechanisms by which the corticosteroids produced the lesions are still purely speculative. One interesting and still unexplainable finding was that males seemed to be more susceptible than females; the opacities were found in 12 males but only 5 females.

The NIAMD and NINDB investigators, who reported the study to the annual meeting of the American Rheumatism Association, emphasized that the opacities do not constitute a major hazard to vision and should not be alarming. To date, no patient has developed serious visual defects. It would therefore seem that in most cases this eye complication by itself would not indicate the need for discontinuing steroids.

Value of gold injections in rheumatoid arthritis confirmed

The distinct value of gold salts in the treatment of arthritis has finally been clearly demonstrated in a British study reported by a recent visiting scientist at the National Institute of Arthritis and Metabolic Diseases. Injections of gold salts were first used in the treatment of rheumatoid arthritis in 1927 and since then have been widely employed by many physicians with varying degrees of success, but few well-controlled studies have been made of this form of treatment. Such studies are not easy to perform since the disease is an extremely variable one and it is very difficult to obtain two similar groups of patients, an experimental group and a control one. This has now been accomplished in the British study and has provided conclusive proof of the value of gold therapy in rheumatoid arthritis.

The double-blind study was carried out in 24 treatment centers in Great Britain under the sponsorship of the Research Subcommittee of the Empire Rheumatism Council. Dr. Eric G. L. Bywaters, who reported the study to the American Rheumatism Association, was one of the participants and is professor of rheumatology at the University of London. He returned to London after a brief stay as a visiting scientist at the National Institute of Arthritis and Metabolic Diseases.

Two hundred outpatients were involved and were divided equally into two groups, comparable in age, sex, and duration of illness. Only patients who had had rheumatoid arthritis for more than 1 year and less than 5 were included in the study, and none had been previously treated with gold salts. The "gold" group was given weekly injections of 50 milligrams of metallic gold (as sodium aurothiomalate) over a period of 20 weeks, while the control group received weekly injections of similar appearance but containing virtually no gold (one one-hundred-thousandths the quantity given the gold group). All received simple supportive measures such as rest, splints, aspirin, and physical therapy.

Improvement in the gold group became noticeably greater than in the control group after the first 3 months and was measured in a variety of ways: (1) functional capacity—more patients became and remained able to carry on normal work and physical recreation; (2) joint involvement—fewer joints became newly affected or reactivated with the disease, while more joints that had been affected became quiescent and remained that way; (3) blood tests—hemoglobin levels and red cell sedimentation rates improved by the sixth month in the gold group and the sheep cell agglutination test became less positive; (4) number of analgesic tablets taken—at the start both groups were taking an equal number of aspirin tablets or equivalent per day. A reduction in aspirin dosage which was considered significant by the investigators was seen in the gold group at the 6th month from the start of the treatment and continued to the 18th month.

X-rays of both groups of patients were also taken at intervals during the study but these did not show any material difference in the two groups.

One of the biggest problems with gold therapy has always been the production of side effects, and these occurred to a significant degree in this study also. Toxic effects, largely dermatitis, were three times more common and were more severe in the gold-treated than in the control group. Complications were noted in about 25 percent of the gold group and 12 percent of the control group. Although the skin reactions were troublesome in a significant number of the cases, the NIAMD visiting scientist reported, various new drugs such as British Anti-Lewisite (BAL—a heavy metal binding compound) and adrenal cortical steroids can reduce the severity of such side effects and lessen the dangers of this form of therapy.

"A later assessment will be made after a further 1-year's followup, but to date the advantage clearly lies with the gold-treated group," Dr. Bywaters concluded.

Present treatment for SLE found valuable

Systemic lupus erythematosus, the so-called Red Wolf disease (Lupus-wolf), has been the subject of a large scale study by a grantee of the National Institute of Arthritis and Metabolic Diseases. Systemic lupus erythematosus (SLE) is a pernicious, multisystem disease entity with certain similarities to rheumatoid arthritis; it is difficult to diagnose because there is no classic disease pattern. Any system may initially be affected and heal; months or years later the same or another area may become involved.

A 10-year, 400-patient study made by Dr. Edmund L. Dubois of the University of Southern California School of Medicine showed that SLE was almost as common as pernicious anemia, leukemia, acute rheumatic fever or serum sickness at the 3,500-bed Los Angeles County General Hospital. One case of SLE was seen for every 14 of rheumatoid arthritis, and 88 percent of the patients were female.

The investigator found that the most effective therapy for milder attacks was bed rest, salicylates and antimalarial drugs. If this treatment failed or if the patients were critically ill or had neurological or renal involvement, corticosteroid treatment was employed. A segment of the study comparing 50 patients treated with dexamethasone with comparable series of patients treated with older adrenocortical steroids showed that the newer steroid, while 20 times more powerful than hydrocortisone and 8 times more powerful than methylprednisolone, brought patients little additional relief. Because of increased side effects, namely edema, hirsuitism, and peptic ulceration, dexamethasone was not preferred.

Although the ultimate cure of systemic lupus erythematosus must await further knowledge of its basic cause, the NIAMD-supported study showed that presently available forms of therapy (salicylates, antimalarial compounds, and corticosteroids) can effectively inhibit for a significant time the grave changes that occur in the disease. The study was reported and was the subject of an editorial in the Journal of the American Medical Association.

Excess body weight has little effect on osteoarthritis

Scientists at the National Institute of Arthritis and Metabolic Diseases (NIAMD) have found that excess body weight bears little if any relationship to the cause of osteoarthritis in mice. The research was reported by Dr. Leon Sokoloff of the Laboratory of Pathology and Histochemistry, and associates, to the annual meeting of the American Rheumatism Association, and has shown that osteoarthritis has a much more complex cause than simply that of extra weight bearing by the joints of the body.

Osteoarthritis is a "wearing away" disease of the joints which is much more common than rheumatoid arthritis but, as a rule, less damaging. The disease seems to result from a combination of aging, damage and normal wear and tear and affects older persons most frequently. Although it has long been supposed that obesity aggravates osteoarthritis in man—presumably by burdening the joints with additional weight—there is little direct evidence of this, and so the present study was done to determine more clearly the relationship between obesity and osteoarthritis.

The NIAMD scientists performed several groups of experiments. In the first one, mice which did not normally become obese were fattened on a diet containing 60 percent vegetable shortening. The mice became 75 percent fatter than litter mates fed a normal diet, but pathological studies of their hind limbs done after 16 months showed that, for the most part, even this severe a degree of obesity did not harm the joints. The same fattening procedure was also used on rats, which are generally less susceptible to joint disease. In these experiments the obese animals did show slightly more arthritis than normally fed litter mates, but their joint disease was very mild.

The most conclusive studies were done with mice belonging to the STR/1N strain. This strain is naturally fat and, in addition, has a high incidence of osteoarthritis. All STR/1N mice develop osteoarthritis by about 1 year of age. To determine whether the animal's weight was directly related to their joint disease, the scientists restricted their weight gain by feeding them a low calorie diet. It was found that the weight restriction had no effect on either the occurrence of osteoarthritis or its severity.

Further proof of the lack of association between obesity and osteoarthritis came from studies of hybrid mice which had resulted from the mating of STR/1N mice (fat, arthritis-susceptible mice) with mice from a thin, arthritis-resistant strain. The hybrids were practically as fat as their arthritic fathers, but had almost as little arthritis as their thin mothers, thus confirming the dissociation between weight and arthritis.

"Under the conditions of these experiments there was no consistent effect of obesity on the development of degenerative joint disease," Dr. Sokoloff reported. Although the obesity-producing diet did slightly influence the development of joint disease in the rats, the results of the other experiments make it unlikely that the effect was simply the mechanical consequence of excessive weight borne by the joint. Possibly, certain metabolic alterations are involved, although no single metabolic abnormality has yet been found.

The NIAMD scientists concluded that the cause of osteoarthritis is a much more subtle and complex biological problem than simple mechanical stress.

Important differences found in joint diseases

Evidence that, contrary to traditional belief, the joint diseases found accompanying ulcerative colitis are basically different from rheumatoid arthritis has been reported by Dr. Currier McEwen and a biostatistician associate, Miss Claire Lingg, both of New York University Medical College. The study supported by a grant from the National Institute of Arthritis and Metabolic Diseases, was reported to the sixth interim scientific session of the American Rheumatism Association. It involved 52 patients and indicated that there are significant differences both in clinical symptoms and in response to blood tests for rheumatoid factor, between persons with rheumatoid arthritis and patients with joint disorders found associated with colitis.

Estimates indicate that about 7 percent of patients suffering from ulcerative colitis also have swollen and inflamed joints, until now thought to be due to rheumatoid disease. In the group of 52 patients studied, 33 had arthritis of peripheral joints, a much higher incidence than was expected.

The Institute-supported investigators found that arthritis accompanying colitis differed from rheumatoid arthritis in several respects: serological reaction for rheumatoid factor was consistently absent; subcutaneous nodules did not appear; affected joints were not of symmetrical distribution; the arthritis was evanescent and not chronic or destructive and therefore did not result in joint destruction or deformity; and prevalence among males and females was about equal whereas in rheumatoid arthritis, three times as many women are affected as men. In a great majority of cases, the appearance of colitis antedated the appearance of arthritis. In a few cases, both diseases started simultaneously or the arthritis preceded the colitis. Flareups of ulcerative colitis frequently coincided with flareups of arthritis.

Fourteen of the 52 patients under study were shown to have spondylitis (arthritis of the spine) which resembled the classical type of ankylosing spondylitis that occurs independent of ulcerative colitis.

Study of Sjogren's syndrome supports autoimmunity concept

A serological study of 21 patients with Sjogren's syndrome, a disorder often accompanied by arthritis, has provided additional support for the concept of autoimmunity as a possible cause of disease. The study, which may throw some light on the basic nature of rheumatoid arthritis, was reported by Dr. Joseph J. Bunim, Clinical Director of the National Institute of Arthritis and Metabolic Diseases, as part of the annual Stoneburner lecture series at the Medical College of Virginia.

The concept of autoimmunity has become popular within recent years to explain the occurrence of certain disease whose etiology is still unknown. According to this concept, it is possible for an individual to become sensitive to substances normally present in body cells and tissues, and to produce antibodies against these substances. The resultant antigen-antibody reactions in the issues are thought to lead to the pathological changes noted in the disease. This concept has been useful in explanations of Hashimoto's disease of the thyroid gland. Individuals with this disorder were found to have circulating antibodies in their serum which reacted with their own thyroglobulin. Presumably, the antibodies were reacting with the thyroglobulin in the thyroid gland and causing the tissue damage characteristic of the disease.

As a result of this work, many studies were begun by various investigators to reexamine other diseases of unknown etiology, in an attempt to discover if they might also be expressions of autoimmunity. At the present time rheumatoid arthritis is being considered as such a disease by many investigators, partly because the "rheumatoid factor" which is present in the serum of rheumatoid arthritics has many of the properties of an antibody. In a related disease, systemic lupus erythematosus, it has been found that the serum contains a whole family of antibodies, some against normal cell nuclei, some against cytoplasm, and others against subcomponents of both nuclei and cytoplasm.

With these findings in mind, Dr. Bunim and his associates at the National Institute of Arthritis and Metabolic Diseases made a comprehensive serological study of patients with Sjogren's syndrome to determine what antibodies might be present in their serum. This syndrome is characterized by hypo-functioning of both the tear and salivary glands and is often accompanied by rheumatoid arthritis. Any two components of the ocular-salivary-arthritic triad are sufficient to establish the diagnosis. Aside from the occurrence of the arthritis, the syndrome is of particular interest because the pathological changes found in both the tear and salivary glands are strikingly similar to those seen in the thyroid glands of persons with Hashimoto's disease.

The NIAMD serological study showed that an abnormally active immunological response was present in patients with Sjogren's syndrome. Almost all the patients gave positive responses to the bentonite flocculation test and sensitized sheep cell agglutination test for rheumatoid arthritis, even though only 8 patients out of 21 had definite clinical signs of the disease. The majority of patients were also found to have a serum constituent that had a specific affinity for cell nuclei, and in this respect they resembled patients with systemic lupus erythematosus. Another interesting finding was the presence of an antibody to human thyroglobulin (14 percent of the cases) which was similar to the one found in Hashimoto's disease.

Dr. Bunim reported that these findings demonstrate that Sjogren's syndrome patients exhibit much greater immunological reactivity than those with rheumatoid arthritis alone, and the diversity of the humoral antibodies may indicate a basic derangement of antibody production.

This NIAMD research thus provides further support for the developing concept of autoimmunity, and indicates that immune mechanisms may be playing an important part in the pathogenesis of these diseases.

DIABETES AND OTHER METABOLIC DISORDERS

The field of diabetes offers many problems for research, for although insulin and diet will control most cases, there are still large gaps in our knowledge of this common metabolic disease. Unsolved questions relate to its basic cause, the many biochemical and physiological changes that take place in body fluids and cells, and the influence of heredity. Of particular interest at the present is the mode of action of the new oral hypoglycemic drugs which have replaced insulin injections in thousands of diabetics. Though these new compounds are widely used, they are not effective in all cases of diabetes, and there is increasing evidence that individual patients may become resistant to one or more of them as times goes on. Undoubtedly, the new drugs have provided a convenient form of treatment but they are not the final answer.

New findings on oral antidiabetic drugs reported

A review of the current status of oral antidiabetic drugs was presented by scientists from the National Institute of Arthritis and Metabolic Diseases, grantees of the Institute, and other investigators at the annual meeting of the American Diabetes Association. Highlights of the meeting included indications that secondary failures of the drugs occur in up to 35 percent of patients, and evidence that prolonged treatment with tolbutamide (in animals) does not exhaust the beta cells of the pancreas as some researchers have feared.

Tolbutamide, the first of the oral antidiabetic drugs, became available in 1957 and since then two others, chlorpropamide and phenformin, have been made available to physicians. At the present time it is estimated that more than one-third of all known diabetics in the United States are now receiving this oral therapy instead of regular insulin injections. Even though these drugs are widely used, the way in which they accomplish their blood-sugar-lowering action is still not fully understood, nor is it known whether the drugs, in the long term, will represent a significant improvement in the treatment of diabetes.

A continuous evaluation of 355 patients treated with the oral drugs over a 4-year period by one group of researchers reporting at the meeting showed that primary failures amounted to approximately 30 percent, and that of the remaining 70 percent of patients, up to 35 percent became secondary failures. They felt that this percentage of secondary failures might eventually be even higher if patient groups are followed for a longer period of time. Some investigators believed that the secondary failures may possibly result from a compensatory increase in the production of insulinase, a hepatic enzyme that degrades insulin in the body.

Other investigators reported that their overall results with phenformin in 107 difficult diabetic patients were not as good as the results which have been reported by physicians who used it in all diabetics. Although the drug was found useful either alone or in combination with insulin, side effects considerably limited it and were noted in half of the patients taking doses over 150 miligrams.

In another reported clinical study the effects of tolbutamide on the levels of serum lipoproteins were investigated, since it was thought that any increases in the beta lipoproteins may parallel the progression of the vascular degeneration seen in diabetes. The study revealed that there was an increase, although a relatively small one, in the beta lipoproteins in patients who have been converted from insulin to the oral drug and who remained "well controlled" as far as their blood-sugar levels were concerned. This raises the question whether the patient who is considered "stabilized" with respect to blood glucose levels is really controlled with respect to his fat metabolism.

In the past, considerable evidence has indicated that tolbutamide facilitates the release of insulin from the pancreas. Therefore it has been a matter of concern that this form of "stimulation," if it occurs chronically or at all, might eventually exhaust the pancreatic beta cells when their number or function is already reduced in the diabetic patient.

Studies of prolonged tolbutamide administration in dogs were reported at the meeting which now indicate that the beta cells do not become exhausted. The animals had three-fourths or more of their pancreas surgically removed in order to diminish their beta cell reserve without producing diabetes, and received repeated intravenous glucose tolerance tests over a period of 13 to 17 months. None of these operated animals became diabetic, and as a group they showed no trend toward an overall decrease in tolerance as compared to control animals.

Tolbutamide did not seem to affect the degree of pancreatic regeneration. A comparison of the estimated amount of remaining pancreas at operation with its appearance and weight at autopsy showed an increase of 1.5 to almost fourfold in both experimental and control groups.

In experiments of a somewhat similar nature, other investigators reported that in rats made "subdiabetic" by alloxan treatment, prolonged tolbutamide administration did not cause permanent deterioration. In fact, some of these alloxanized animals insular function improved.

Insulin antagonists found in untreated diabetes

The presence of substances antagonistic to insulin in the plasma of patients with diabetes mellitus who have never received insulin therapy has been shown in recent studies by Dr. James B. Field, Clinical Endocrinology Branch, National Institute of Arthritis and Metabolic Diseases. These studies shed provocative light on an important possible cause of diabetes other than pancreatic inability to produce insulin.

The likelihood that many cases of diabetes are due to substances in the patient's body which interfere with provision of an effective insulin concentration to peripheral tissues has been considered by endocrinologists for many years. A cause of diabetes of this sort is under investigation because numerous diabetic patients require more than 40 units of insulin a day, the level needed by a patient whose pancreas has been removed in the treatment of some other disease and whose diabetes is thus due to his inability to produce his own insulin.

Inhibitors or antagonists to the action of insulin having the properties of antibodies have previously been found by Dr. Field and other investigators in the plasma of patients with chronic insulin resistance requiring amounts of insulin in excess of 200 units per day. Temporary insulin resistance, accompanied by the presence of increased amounts of inhibitors, has also been found in diabetic acidosis or coma and during infection. In general there has been no good correlation between the titer of insulin antibody and a patient's daily insulin dosage.

The recent studies of Dr. Field differ from previous observations in that insulin antagonist was detected in the plasma of two of four new diabetic patients prior to insulin therapy, indicating the presence of a substance interfering with the action of insulin which is not an antibody elaborated in response to administered insulin. Clinically, there were no distinguishing features between the two cases with antagonist and those without. They all had high blood sugars, large amounts of sugar and ketone bodies in the urine without severe acidosis and required insulin for control of their diabetes in approximately equal amounts. Inhibitor could no longer be detected once the diabetes was controlled.

Detection of this apparently new type of insulin antagonist in the NIAMD studies provides a lead for further investigation of a variety of factors affecting insulin production, binding, transport, and action at the peripheral tissue level. The possibility exists that the antagonist is a harmone of pituitary origin, perhaps related to growth hormone. The studies, and a review of factors affecting insulin action, were reported by Dr. Field in the Journal of the American Diabetes Association.

Methol found to have hormonelike activity

Menthol, the substance that gives peppermint its characteristic odor, has been found to have an effect similar to that of the female sex hormone progesterone on the metabolism of galactose. This discovery, by scientists at the National Institute of Arthritis and Metabolic Diseases, indicates that menthol may be another rare example of a nonsteroidal compound that produces some of the same physiological effects as a hormone.

Menthol's hormonelike effect became apparent during studies of galactosemia, a relatively rare hereditary disorder of children. Infants with this disease are unable to tolerate galactose, a sugar present in milk, since they lack one of the enzymes necessary for galactose metabolism. If milk is allowed to remain in their diet, it quickly creates a toxic condition leading to mental retardation, cataract formation, liver damage, and early death.

The basic nature of the disease was discovered in 1955 by scientists at the National Institute of Arthritis and Metabolic Diseases who first made the biochemical diagnosis and pinpointed the exact enzyme that was deficient. Further studies of the disease led to the discovery that injections of the hormone progesterone enabled galactosemic children to metabolize at least some galactose.

Apparently the hormone enables the body to overcome the enzymatic block. This finding was reported last year and set an important precedent for research on other metabolic disorders caused by enzyme deficiencies.

The hormone-like activity of menthol was discovered by accident during detailed in vitro studies of progesterone's effect on galactose metabolism. Menthol was being employed to study some of the reactions when it was noted that the compound had the same ability to stimulate galactose metabolism as progesterone. Oral doses of menthol were then tried in two galactosemic children and enabled them to metabolize the same amount of galactose as they would have with progesterone injections. These findings were reported at the Federation meetings by Drs. T. D. Elder, S. Segal, E. S. Maxwell, and Y. J. Topper of NIAMD.

The therapeutic implications of the findings have yet to be explored since only tracer doses of galactose have been used in the clinical trials. Also, the mechanism by which either progesterone or menthol exert their effects in vivo is not yet known. Menthol may prove to be of particular value in further NIAMD studies of this phenomenon since the menthol molecule is a much smaller and simpler one than that of progesterone.

New blood test developed for galactosemic children

A new blood test for monitoring how completely milk and milk-containing foods have been eliminated from the prescribed diet of children with galactosemia has been developed by Drs. Henry Kirkman and Elizabeth Maxwell, of the National Institute of Arthritis and Metabolic Diseases. (Dr. Kirkman is now at the University of Oklahoma Medical School.) The test measures the amount of galactose-1-phosphate present in red blood cells, and since this substance is thought to be the most important toxic agent in the disease the test will be valuable in managing galactosemic patients.

The exact biochemical defect in the disease was first demonstrated by Dr. Herman Kalckar and associates at NIAMD in 1956, who found that galactosemic individuals lacked a single enzyme necessary to completely metabolize galactose. Because of this inherited enzyme deficiency, galactose-1-phosphate accumulates in the blood and tissues and produces the characteristic symptoms.

Although diagnosis now presents little difficulty (Dr. Kalckar's work provided a specific biochemical test for the disease) keeping galactosemic children under strict dietary control is a continuing problem. It is difficult to find processed foods which contain no milk or milk products and the clandestine ways children have of getting food often result in unsuspected breaks in their prescribed diet.

The new test now provides a way to determine how much galactose, if any, the child is getting and is sensitive enough to indicate a break in the diet as short as 1 day. It can be performed in several hours with equipment usually found in a medium-sized hospital or public health center and uses the same reagents as the diagnostic test developed by Dr. Kalckar. These reagents are presently available commercially from the Sigma Biochemical Supply Co. in the form of a diagnostic kit.

The NIAMD scientists reported on the development of the new test in the Journal of Laboratory and Clinical Medicine.

Special diet prevents mental effects of phenylketonuria

Convincing evidence that a special diet can prevent or delay severe mental deficiency in children with phenylketonuria (PKU) has now been provided by a grantee of the National Institute of Arthritis and Metabolic Diseases. His study, involving every case of PKU reported up to December 1959, shows that a child's IQ permanently drops 5 points for every 10 weeks after birth that the diet treatment is delayed.

Phenylketonuria is an "inborn error of metabolism" whose most disastrous consequence is severe mental retardation. The disorder is caused by the lack of a single enzyme in the body, and an enzyme needed to convert phenylalanine, one of the amino acids, into tyrosine, another amino acid. Because the enzyme is lacking, this metabolic "step" is blocked and abnormal amounts of phenylalanine accumulated in the blood.

Previous studies by other investigators have shown that although there is no cure for the basic defect, a diet low in phenylalanine prevented to some extent the mental retardation of PKU. Until now, however, the degree of effectiveness of the diet on the mental deficiencies had been uncertain because of small sizes of diet-treated patient series and varying degrees of mental retardation normally found in the disease.

Dr. W. Eugene Knox, an NIAMD grantee at Harvard Medical School, has pooled and compared the results of all reported treated cases of PKU and has assessed the value of the treatment by comparing results of the treated patients of different ages with the natural history of the disease in untreated patients. He found that in a group of 43 patients treated before age 3, there were 18 times as many with IQ's above 60, twice as many with normal electroencephalograms, and fewer with seizures than in a group of 20 that had received no dietary therapy. Those treated before 16 months, compared with those treated between 16 months and 3 years of age, had 4 times as many with IQ's above 60 and fewer seizures. The early treated group also had more normal electroencephalograms. Forty-three patients with PKU over 3 years of age were treated without impressive changes in their mental and neurological state.

For the whole group, the NIAMD supported investigation showed that the final IQ was negatively correlated with age at the start of treatment in a highly significant manner. Over the 3-year period studied, a minimal loss of nearly 5 points in IQ occurred each 10 weeks that treatment was delayed. This finding points to the obvious importance of diagnosis of PKU as soon as possible after birth. To this end a relatively simple diagnostic test was developed last year by Dr. Bert LaDu of NIAMD in Bethesda; the test can be performed in 10 minutes on finger-prick samples of blood.

This study "provides the final evidence that phenylalanine in some way causes these central nervous system abnormalities. The primary enzymatic defect leading to accumulation of phenylalanine is therefore linked through a causal chain to the mental deficiency. This means in practice that treatment to reduce accumulation of phenylalanine in patients with phenylketonuria should not be denied." Dr. Knox reported. The work was reported in Pediatrics.

Rapid screening test for Wilson's disease developed

A spot test for detecting children who may develop Wilson's disease later in life has been developed by grantees of the National Institute of Arthritis and Metabolic Diseases. The test is simple and rapid and measures the amount of the plasma copper protein, ceruloplasmin, in a blood sample. Its routine use as a screening procedure may make it practicable to prevent or delay the onset of the symptoms and signs of Wilson's disease.

Wilson's disease is believed to result from abnormal copper metabolism and is characterized by an hereditary deficiency of ceruloplasmin and progressively fatal degeneration of the liver. Excessive amounts of copper accumulate in the liver, brain, and urine, and the urinary excretion of amino acids also increases. It is not yet clear what the relation is between these metabolic changes, but it appears that the accumulated copper is responsible for the pathologic changes seen in the disease.

The NIAMD grantees believe that the chief clinical value of the new test will lie in screening apparently healthy children to detect those who are deficient in ceruloplasmin. This is important, since the signs and symptoms of the disease rarely occur before the age of 7 or 8 years, although the deficiency in ceruloplasmin appears to be present from birth. Therefore, if latent Wilson's disease, or hypoceruloplasminemia, is demonstrated measures, may be instituted to minimize the absorption of copper from the diet, and to promote the excretion of copper already absorbed.

The basis of the test is that ceruloplasmin catalyzes the oxidation of the polyamine, paraphenylenediamine (ppd). The test is made on a sample drop of either plasma or serum which is placed on a paper strip treated with ppd dihydrochloride. The intensity of the blue spot which then appears under the test sample is compared with that made by a sample of normal serum or plasma; it is possible to determine whether the sample contains more or less than about 20 milligrams of ceruloplasmin per 100 milliliter of plasma or serum. The normal value is 18 to 35 milligrams per 100 milliliter. (Prepared paper strips, capillary tubes, and standard serum for clinical testing are now available from the Ortho Research Foundation, Raritan, N.J.)

Ceruloplasmin levels are naturally low in newborn infants but they appear to be consistently above 18 milligram per 100 milliliter by the second month of life. Therefore, it seems that the spot test can be used as a screening procedure in infants at any time after the age of 3 months, perhaps most conveniently at a time when routine immunizations are given, the NIAMD grantees reported.

"Since Wilson's disease is an uncommon condition and practically the only cause of persistent deficiency of ceruloplasmin, usually in the range of 0 to 15 milligram per 100 milliliters of serum, confirmatory studies, including quantitative analysis for ceruloplasmin, can be made in the relatively small number of children in whom positive results of the spot tests are obtained. In children who show persistent ceruloplasmin deficiency, Wilson's disease is reasonably certain to develop, but early diagnosis may make it possible to prevent or delay the appearance of hepatolenticular degeneration," the investigators concluded.

The development of the spot test was reported in the American Journal of Medicine by Drs. Philip Aisen and Julian B. Schorr, Anatol G. Morrell, Ruth Z. Gold, and Dr. I. Herbert Scheinberg, Albert Einstein College of Medicine and Bronx Municipal Hospital Center, and the Columbia University School of Public Health and Administrative Medicine, New York, N.Y.

Diet, not heredity, may cause hemochromatosis

Hemochromatosis and hemosiderosis, disorders in which abnormal amounts of iron are deposited in body tissues, have been thought to be examples of inborn errors of metabolism. A comprehensive study of 211 cases of these disorders by grantees of the National Institute of Arthritis and Metabolic Diseases (NIAMD) has now indicated that alcoholism and nutritional factors, rather than genetic ones, are etiologically implicated.

Hemochromatosis, or bronze diabetes, is a rare disease that is usually ascribed to an inborn error of metabolism. It is characterized by widespread deposits of hemosiderin (an iron-protein complex that is probably a storage form of iron) and presumably results from exaggerated absorption of iron from the intestinal tract. The pigment deposits cause degenerative and fibrotic changes in the involved organs, particularly the liver and pancreas, and lead to the classic triad of bronzed skin, diabetes, and cirrhosis of the liver. Hemosiderosis, a closely related disorder, is distinguished from hemochromatosis by the lack of tissue damage in the organs even though pigment deposits are present.

The present NIAMD-supported study of 211 autopsied cases of hemochromatosis and hemosiderosis was undertaken at Boston City Hospital and reported by Drs. Richard A. MacDonald and G. Kenneth Mallory, of the hospital, Harvard Medical School and Boston University School of Medicine, in the AMA Archives of Internal Medicine.

The autopsied cases of these diseases occurred in 25,295 post mortems between the years 1917 and 1956 and were separated into 3 groups according to pathological criteria; there were 57 cases of hemochromatosis, 104 cases with a slight amount of hemosiderin in various organs, classified simple hemosiderosis, and an intermediate group of 50 cases, classified advanced hemosiderosis. From careful analyses of the autopsy diagnoses, clinical records, and all available microscopic sections the investigators pieced together a disease pattern which has led them to suspect that alcoholism and nutritional factors, rather than genetic ones, are of prime etiological importance.

Originally, one of the bases on which hemochromatosis was considered an inborn error was the reported appearance of the disease in two or more members of the same family. In the present series of over 200 cases, however, there was only 1 patient known to have a sibling with hemochromatosis.

Of greater significance, the NIAMD grantees believe, was their finding that hemochromatosis and hemosiderosis frequently occurred together with fatty nutritional (alcoholic) cirrhosis, and that 85 percent of patients with hemochromatosis whose clinical records were available used alcohol to excess. Three-fourths of those who denied alcohol had a history of a grossly inadequate diet. Among the hemochromatosis patients 45.6 percent had either fat in the liver or cirrhosis with fat, in addition to pigment cirrhosis; among the advanced hemosiderosis patients 86.2 percent of the cirrhotic ones had elements of fatty nutritional cirrhosis as did 28.5 percent of noncirrhotic ones; and among the simple hemosiderosis patients 69 percent of the cirrhotic ones had fat in the liver as did 32.5 percent of the noncirrhotic ones.

No definitive differences between the three groups were found when clinical and pathological features were compared, suggesting that the three groups were not sharply distinct entities but were variants of a single condition. It was also noteworthy that transfusions were not a significant factor in the study. In most patients excess iron in the tissues appeared to have been the result of absorption from the diet.

The histologic picture of pigment cirrhosis was often consistent with that resulting from a preexisting fatty nutritional cirrhosis in which fat had been mobilized from the liver, the NIAMD grantees reported, and they believe that the "idiopathic" type of hemochromatosis may be a variant of nutritional cirrhosis, in which the same factors that contribute to the cirrhotic process lead to iron absorption. Other cases of hemochromatosis may be due to a combination of factors, such as anemia or hematologic disease causing excessive iron absorption, with transfusion or orally administered iron further contributing to the amount of iron in the tissues. In addition, they concluded, there may coexist factors that contribute to, or in themselves lead to, cirrhosis.

Ether anesthesia found to cause metabolic changes

Grantees of the National Institute of Arthritis and Metabolic Diseases have found that ether anesthesia produces marked changes in normal carbohydrate metabolism. Their research indicates that ether inhibits specific metabolic pathways and suggests that it may be more advantageous to feed surgical patients within travenous fructose rather than glucose since fructose metabolism is less affected than is the metabolism of glucose.

It has been known for many years that ether anesthesia affects carbohydrate metabolism, increasing the blood levels of glucose, pyruvic acid, and lactic acid. Numerous investigators have also noted increases in serum inorganic phosphorus during ether anesthesia. What has not been clear, however, is whether the anesthetic causes a generalized depression of enzymatic processes or inhibits only specific metabolic pathways.

In an attempt to clarify ether's effect on carbohydrate metabolism NIAMD grantees have studied the metabolism of two sugars, fructose and glucose, in anesthetized subjects. The subjects were all volunteer patients without metabolic disorders, and since there was no surgery performed during the anesthesia the metabolic changes could be attributed to ether alone. Both glucose and fructose tolerance tests were performed under anesthesia, and the results were compared with those obtained in the same patients on the days preceding and following the administration of ether.

As expected, the levels of glucose, pyruvic acid, and lactic acid were all increased during anesthesia. However, in contrast to the metabolic disturbance found after surgery, most of the changes noted did not persist; they returned to the control range within 24 hours. After surgery, these changes are known to persist for at least 48 hours. The NIAMD grantees also found that during anesthesia intravenous infusions of glucose could not be assimilated as rapidly as they normally had been. Infusion of fructose, on the other hand, could be assimilated just as rapidly under anesthesia as they were under normal conditions. Since the metabolism of glucose involves different pathways from those of fructose, the investigators interpret the results as indicating that ether inhibits only certain metabolic pathways without causing a generalized interference with biochemical processes.

The scientists supported by NIAMD believe that these metabolic alterations found during anesthesia suggest several improved means of managing patients during surgery. Preanesthetic administration of carbohydrate may be indicated since a high content of hepatic glycogen is known to protect the liver from damage during anesthesia. Also, the use of fructose may have the advantage of being more protective than glucose since studies by other investigators have shown that in both normal and diabetic patients the liver removes intravenously administered fructose twice as rapidly as it does glucose in comparable situations, and fructose tolerance was relatively unimpaired in this anesthesia investigation.

"In addition, the results of the present study indicate intravenous fructose is assimilated more rapidly than intravenous glucose by subjects during ether anesthesia. Consideration of these findings may be important for the optimal alimentation of surgical patients if the present trend continues toward longer operations and more operations in the geriatric age group," the investigators concluded.

The study was reported by Drs. W. R. Drucker, Christine Costley, Robert Stults, William D. Holden, James Craig, Max Miller, Nancy Hofmann, and Hiram Woodward, of Western Reserve University, Highland View Hospital, and the University Hospital of Cleveland, Cleveland, Ohio, in the journal Metabolism.

Pituitary reserve function measured by new test

A new method to determine the "reserve capacity" of the pituitary gland for secreting ACTH (adrenocorticotropin) has been developed by grantees of the National Institute of Arthritis and Metabolic Diseases. The new test indicates how well the pituitary is able to respond to above-normal demands for ACTH, as in stress, injury or infection, and may help clarify the role played by this master gland in various endocrinological disorders. The development of the test was a logical continuation of research done by Dr. Roy Hertz of the National Cancer Institute on amphenone, a compound which inhibits the production of cortisol by the adrenal gland.

The ideal way to study pituitary secretion of ACTH would be to measure the levels of the hormone itself in the blood, but since available methods are not sufficiently sensitive to measure circulating ACTH (under most physiologic conditions) an indirect type of measurement must be used. This has been made possible in the new test by employing an agent known as SU-4885[1] (an analogue of amphenone) to inhibit the synthesis of cortisol (hydrocortisone) by the adrenal gland. The falling level of cortisol then stimulates the pituitary to "compensate" by producing more ACTH and the additional ACTH, in turn, causes the adrenal gland to secrete large quantities of 11-desoxycorticosteroids which can be readily measured in biologic fluids as 17-hydroxycorticoids.

Thus, in normal subjects, SU-4885 induces a rise in total blood and urinary corticoids. Since this response to SU-4885 is dependent upon a rise in ACTH secretion, the compound affords (in patients with no frank adrenal insufficiency) a sensitive means of testing the reserve capacity of the pituitary gland to secrete ACTH. To explore the possible diagnostic use of the phenomenon, the NIAMD grantees studied the effects of SU-4885 in 71 patients whose endocrinological status had been clearly defined by conventional methods.

In certain endocrine states the results obtained were as anticipated but in others revealing information was derived as to the state of pituitary-adrenal integrity. For example, in Addison's disease (adrenal insufficiency) there was no appreciable increase in urinary 17-hydroxycorticoids; in hypopituitarism no increase in the already subnormal excretion of urinary 17-hydroxycorticoids was noted; in Cushing's disease all patients with active adrenal hyperplasia showed responses which were greater than the average response of normal subjects; some patients with a chromophobe adenoma of the pituitary had normal responses and some did not, indicating that in this condition there is frequently, but not invariably, damage to the ACTH-secreting mechanism so that varying degrees of hypoadrenocorticism result; in acromegaly some of these patients had limited capacities to secrete ACTH under test conditions; all patients with cachexia exhibited "limited pituitary reserve," indicating that sever malnutrition may frequently be associated with impairment of the pituitary capacity to respond to the demands of a disease or stress situation.

The results obtained in a variety of clinical situations appear to substantiate the validity of the SU–4885 test, and the NIAMD grantees concluded that it now provides a means of testing the reserve capacity of the pituitary-adrenal system to satisfy extraordinary physiologic needs for cortisol. The findings were published in the Journal of Clinical Endocrinology and Metabolism by Drs. G. W. Liddle (formerly of the staff of the National Heart Institute), H. L. Estep, J. W. Kendall, W. C. William, and A. W. Townes of Vanderbilt University School of Medicine, Nashville, Tenn.

Germ-free animals used to study nutrition

The use of germ-free animals at the National Institute of Arthritis and Metabolic Diseases (NIAMD) has helped to clarify the role played by man's intestinal bacteria in supplying essential nutrients.

At the recent Fifth International Congress on Nutrition held in Washington, D.C., Dr. Floyd S. Daft and Ernest G. McDaniel reported on their studies of the growth-promoting effects of penicillin and ascorbic acid in rats, and the production of folic acid by gastrointestinal bacteria.

Earlier studies showed that both penicillin and ascorbic acid could prevent a deficiency in pantothenic acid, an essential B vitamin, in conventionl rats, but the exact mode of action of these compounds had not been clear. In the reported studies, germ-free rats were fed a pantothenic-free diet containing either 200 milligrams percent penicillin or ascorbic acid at a level of 2 percent in the diet. Neither of these compounds prevented the B vitamin deficiency in the germ-free animals, indicating that the previously observed growth-promoting effects of these compounds are mediated through their biochemical action on intestinal bacteria.

The NIAMD investigators also clarified aspects of folic acid deficiencies. It is well known that conventional rats do not require a dietary source of folic acid. However, symptoms of folic acid deficiency can be produced in rats on a folic-free diet, if sulfa drugs are administered. This suggests that folic acid is ordinarily made available to the host animal by bacteria in its gastrointestinal tract and that this essential vitamin is no longer synthesized during suppression of the intestinal flora by sulfonamides.

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[1] 2-methyl-1,2-bis(3-pyridyl)-1-propanone.

The germ-free studies confirmed this hypothesis by showing that germ-free rats develop severe folic deficiency after about 50 days on a folic-free diet. Normal growth stops, severe anemia develops, and the animals die if not treated. These results indicate that the rat does have a requirement of folic acid which, under normal circumstances, is satisfied through synthesis of this essential nutrient by the intestinal bacteria. Such studies furnish significant analogies for the elucidation of the role of intestinal microflora in the nutrition of man.

"Nibbling" has specific effects on regulation of metabolism

The laboratory rat is a nibbler while man is an eater of full meals, and therein lies a difference that can have a marked effect upon experimental studies of obesity, atherosclerosis, and diabetes. This has been reported by grantees of the National Institute of Arthritis and Metabolic Diseases who found that the difference in the rate of ingestion between nibbling and eating spaced, full meals affects the regulation of metabolism of fat, carbohydrate, and protein as well as the synthesis or release of several protein hormones. As a result of their findings, the grantees believe that experimental animals such as the rat should be trained to eat full meals as men do if they are to be used in studies of human disease.

It has long been assumed that as long as food enters the gastrointestinal tract, no matter how it gets there, an animal would handle it in the same way. The NIAMD-supported studies, however, comparing body composition and metabolic activities of force-fed animals with those of animals eating ad libitum, show that great differences in intermediary metabolism are produced by the manner of eating. In rats, meal eating as contrasted with nibbling resulted in (1) a 50- to 100-percent increase in the body fat, (2) a 10- to 20-percent decrease in protein synthesis, (3) a threefold increase in glucose-6-phosphate dehydrogenase activity, (4) a decreased I^{131} uptake by rat thyroid and diminished thyrodial I^{131} decay, (5) development of diabetes in partially pancreatectomized rats, and (6) enhanced atherogenesis in monkeys and chickens.

These findings, the grantees believe, indicate that full-meal eating is associated with a more economical use of calories, leading to obesity and that meal eating differentially affects the traffic over alternate metabolic pathways. Also, the rate of thyroid stimulating hormone (TSH) release by the pituitary may be decreased by meal eating.

"It appears unimportant at this time to determine whether man is basically a converted nibbler, but it does appear that extremely significant information would be obtained if it were found that man reacts to meal eating as contrasted to nibbling as does the rat. If man does react in this manner, it is quite possible that a number of diseases associated with abnormalities in fat, protein, and carbohydrate metabolism may be caused or aggravated by eating habits * * * it appears to us that animal experimentation that is designed to explore diseases and metabolic abnormalities which afflict man should use the feeding patterns of man," the investigators concluded.

The work was reported by Drs. Clarence Cohn and Dorothy Joseph, of the Department of Biochemistry, Medical Research Institute, Michael Reese Hospital, Chicago, Ill., in Metabolism.

GASTROENTEROLOGY

Peptic ulcer, ulcerative colitis, ileitis, and other diseases of the digestive system afflict thousands of Americans, in many cases causing death or prolonged and expensive hospitalization. Their importance is reflected in the fact that diseases of the digestive system rank second only to heart disease in the number of illnesses requiring attendance by a physician. These diseases are only beginning to get the research attention they deserve since too few investigators had been interested in them in the past. The momentum is increasing, however, due to the availability of new techniques such as radioisotope studies, improved methods of determining gastric secretions, and the use of specialized motion picture equipment to photograph the activities of internal organs during health and disease.

Research reveals direct cause of ulcer pain

Studies of more than 500 ulcer patients by grantees of the National Institute of Arthritis and Metabolic Diseases have shown that, contrary to common belief, ulcer pain is not caused by the direct chemical irritation of tissue by hydrochloric acid but results from a disturbance in the motor activity of the stomach and duodenum.

The investigators used a variety of techniques to clarify the mechanism of ulcer pain. One was the acid test, the instillation of hydrochloric acid into the stomachs of patients with active ulcers who had experienced pain within the previous 24 to 48 hours, or who were having spontaneous pain at the time of the study. Contrary to the 85–90 percent of positive results reported by other investigators, the NIAMD-supported group found positive results in only 36 percent of the patients, that is, only about a third of them developed typical ulcer pain or experienced continuation or accentuation of spontaneous pain.

Because of this discrepancy, the investigators were led to make fluoroscopic studies of the motor activity of the stomach and duodenum in ulcer patients during periods of pain. Using a new fluorocinematographic device developed especially for this research, the grantees were able to make X-ray motion pictures of gastrointestinal motor activity over a prolonged period of time. Concurrently, they recorded intraluminal pressures in various parts of the stomach and duodenum and correlated the pressure changes with gastric movements.

They found that although duodenal ulcer pain was accompanied by a significant increase in motility, at the same time there was a significant delay in gastric evacuation. The coordination of motor activity that serves to pump out material from the stomach was temporarily lost, probably because of increased resistance at the pyloric sphincter. In contrast, no alterations in motor activity were found in ulcer patients who were not having pain. In most instances pain relief occurred spontaneously when evacuation activity was resumed. This may account for the fact that pain often disappears after food is ingested and resting motor activity becomes converted to evacuation motor activity. (Similarly, the relief of pain following vagotomy and cholinergic blocking agents may be related to their inhibitory effect upon gastrointestinal motor activity.)

The authors feel that the mucosal engorgement accompanying the ulcer may lower the threshold to hydrochloric acid, permitting the acid and perhaps other stimuli to initiate the reflex disturbance in motor activity which is the direct cause of the pain.

These NIAMD-supported gastroenterological studies are continuing. This particular phase was reported in the Annals of Internal Medicine by Drs. E. C. Texter, Jr., G. R. Vantrappen, H. P. Lazar, E. J. Puletti, and C. J. Barborka, of the Veterans' Administration Research Hospital, Passavant Memorial Hospital, and Northwestern University Medical Center, Chicago, Ill.

Closing mechanism between stomach and esophagus identified

The long-disputed mechanism by which food in the stomach is prevented from returning through the esophagus during digestion has been demonstrated independently by two groups of NIAMD-supported investigators. Their studies indicate that an "intrinsic sphincter mechanism exists in the lower portion of the esophagus, in the area where it is attached to the stomach. A circular bundle of esophageal muscle fibers apparently closes off the esophagus by contracting, and although this mechanism is not anatomically distinct, the area has definite characteristics which are different from the remainder of the esophagus. Determination of its exact location is of considerable value to the surgical management of patients with disorders of the esophagogastric junction.

Using a device for simultaneously taking fluoroscopic motion pictures of the esophagus while measuring its intraluminal pressure, NIAMD grantees at Northwestern University Medical Center have demonstrated that approximately the distal inch of the esophague acts as a physiological sphincter (a functional closing mechanism). A high-pressure zone occurs in this segment of the esophagus and apparently results from the continuous contractions of the circularly arranged muscle fibers. The pressures in this segment are such that during each phase of respiration the whole zone or part of it acts as a barrier against reflux.

Through surgical studies on experimental animals, NIAMD grantees at the University of Virginia have now established the intrinsic nature of the mechanism. The sphincteric action is in the esophageal segment itself and is not dependent upon such extrinsic mechanical factors as the movements of the diaphragm. When the terminal segment of the esophagus was resected or surgically isolated there was a loss of reflux control; control returned when the isolated segment was restored to its normal position. The surgical researchers have also devised an operation which offers promise as a reconstructive measure in patients who have lost function in the lower portion of the esophagus or had it removed. The surgeons produce an artificial extrinsic sphincter by wrapping a flap of the diaphragm around the esophagus where it joins the stomach. Respiratory motions then cause the flap to close off the stomach.

The Northwestern NIAMD grantees, Drs. G. Vantrappen, E. Clinton Texter, Jr., Clifford J. Barborka, and J. Vandenbroucke reported on the work in the American Journal of Medicine, and the work of the Virginia investigators was reported by Drs. Phyllis Ingram, James Respess, and William Muller, Jr., in Surgical Forum.

Severity of liver disease indicated by new test

A new ammonium tolerance test which can aid in evaluating liver disease has been developed by an Institute grantee. The new test is simple and safe and consists of administering a provocative oral dose of ammonium citrate and then measuring the resultant levels of blood ammonia. It provides a sensitive index of the existence of portal-systemic shunts and a method of estimating the severity of parenchymal liver disease.

Studies of the metabolism of ammonia in man during the past few years have made it clear that elevations of ammonia concentration in the peripheral blood are dependent almost invariably upon either severe degrees of hepatic parenchymal disease or due to the existence of spontaneously developed or surgically constructed shunts around the liver.

The present study of the effects of the diagnostic value of an oral dose of ammonium citrate was conducted in patients with various known degrees of liver damage. Some of the patients in each group had demonstrable shunts in the form of esophageal varices. Five to ten grams of ammonium citrate were administered to the patients and their peripheral venous blood ammonia concentration was then measured at intervals of 30, 60, 120, and 240 minutes. Toxic manifestations other than occasional mild cerebral symptoms were not observed.

The NIAMD-supported investigator, Dr. William V. McDermott, Jr., of Harvard University, reported in Surgical Forum that in patients with severe liver disease the induced hyperammoniemia persisted for many hours, probably because of defective urea synthesis. It was not possible solely on the basis of the rate of disappearance of blood ammonia, however, to determine consistently the presence or absence of varices in these patients.

On the other hand, patients with normal or well compensated liver function showed no appreciable rise in blood ammonia levels unless a portal shunt existed. If esophageal varices were present, then there was a rapid rise in blood ammonia levels within 30–60 minutes, followed by a rapid fall over the next 2 to 3 hours. "In several instances this method of defining the presence or absence of esophageal varices has proved to be more accurate than radiographic techniques," the NIAMD grantee concluded.

Alcohol's effect on liver clarified

Studies of alcohol's effect on liver tissue have shown that alcohol (ethanol) stimulates the synthesis of fatty acid in the liver. This finding, confirmed by both *in vitro* and *in vivo* studies, helps explain the production of a fatty liver in chronic alcoholism.

Although fatty degeneration of the liver has long been known to be associated with chronic alcoholism, the mechanism by which alcohol produces this effect has not been clear. Now, both in vitro and in vivo animal studies by grantees of the National Institute of Arthritis and Metabolic Diseases have contributed substantially to the understanding of this action. The studies have shown that ethanol in divided and moderate doses causes the concentration of fatty acid in the liver to increase by indirectly supplying DPNH, an enzymatic cofactor involved in fatty acid synthesis. The finding was reported by Drs. C. S. Lieber, L. M. DeCarli, and Rudi Schmid, Boston, Mass., to the recent meeting of the American Society for Clinical Investigation at Atlantic City, N.J.

The investigators injected tracer doses of acetate-1-C^{14} into male rats and then, after feeding the animals either glucose or ethanol, measured the amount of acetate-1-C^{14} incorporated into hepatic fatty acids. The ethanol-treated rats, in comparison to their glucose-fed littermates, showed not only an increase in the concentration of total hepatic fatty acids but also a 40-percent increase in the incorporation of C^{14}. Further in vivo studies confirmed this stimulatory effect on fatty acid synthesis in the liver.

To uncover the mechanism of this stimulation, in vitro studies were done on liver slices incubated in ethanol, and demonstrated a three- to eight-fold increase in the incorporation of acetate-1-C^{14} into fatty acids. In contrast, ethanol had no effect on fatty acid synthesis in adipose tissue.

The NIAMD-supported scientists found that ethanol's effect is due to an increased formation of DPNH which occurs in the liver when ethanol is oxidized. (DPNH in its oxidized form, DPN, is a cofactor required by many enzymes and is intimately involved in fatty-acid synthesis.) Thus, as the ethanol is oxidized, the amount of available DPNH increases and this in turn leads to an increase in fatty acid synthesis. These findings, both in the intact animal and in liver slices, now provide an explanation for the common finding of fatty livers in patients with chronic alcoholism.

An alternate explanation for the stimulating effect of ethanol on hepatic fat synthesis has also been proposed elsewhere by Dr. B. B. Brodie and colleagues of NHI. According to this view, large single doses of alcohol interfere with the normal endocrine (pituitary) control of fat transport and result in the mobilization of excessive quantities of fatty acids from the adipose tissues of the rat. These free fatty acids circulate to the liver where they are recombined with glycerol and deposited in the parenchyma as triglycerides.

BASIC RESEARCH

There is a continuing requirement for basic research by the Institute, for despite the gratifying progress that is being made in controlling some of the chronic diseases there is still far too little known about their fundamental cause and nature. Much of this needed knowledge can only come from basic research; it is the common thread that runs through the fabric of all the medical sciences. Many of the studies now being pursued at the Institute have no immediate application to the treatment of a particular disease, but they are vitally necessary to provide basic facts about living systems. Of increasing interest are Institute studies in the fields of epidemiology and biometrics, which are concerned with the reasons why some population groups are more or less susceptible to disease than others. A thorough analysis of these reasons—nutritional, climatic, genetic, etc.—promises to provide scientists with a better understanding of many diseases.

Major finding on hormone action reported

Studies by Drs. K. Lemone Yielding of the Institute's Arthritis and Rheumatism Branch, and Gordon M. Tomkins, Laboratory of Biochemistry and Metabolism, have shown that certain female sex hormones can alter the molecular structure of a key catalyst in mammalian cell metabolism, by fragmenting it into four smaller, catalytically altered molecules. This is the first time that a hormone has been found to affect directly the physical structure of an enzyme; previous studies by other investigators have suggested that hormones exert their biochemical influences by participating chemically in metabolic reactions, undergoing an oxidative or reductive change.

As indicated by the NIAMD studies, the reversible physical inactivation of a strategically placed cell enzyme determines the direction which the cell's metabolic processes will take—toward energy-yielding chemical breakdown, or toward cell-building protein synthesis. This finding of molecular alteration is the first concrete illumination of a basic regulatory mechanism which determines protein synthesis and, indirectly, reflects on associated cell growth or cell proliferation.

The studies reported describe the effect of four steroid hormones on crystalline glutamic dehydrogenase (GDH), an important enzyme which facilitates the energy-yielding chemical degradation of glutamic acid. The absence or inactivation of this enzyme tips the scales toward the diversion of glutamic acid to protein synthesis by the cell.

In in vitro experiments Drs. Yielding and Tomkins found that diethylstilbesterol, estradiol, and progesterone, all belonging to the group of female sex hormones, inhibited the normal GDH reaction. Further investigation demonstrated that the hormones promoted dissociation of the large GDH enzyme molecule, which has a molecular weight of 1 million, into four subunits of molecular weight of 250,000. These smaller molecules were enzymatically inactive with respect to GDH activity. Inactivation of the enzyme was reversed in the presence of adenosine diphosphate, a normal cell metabolite. Cortisone, another steroid hormone tested, did not affect the molecular architecture of GDH and correspondingly did not interfere with chemical degradation of glutamic acid. This selective inhibition by female sex hormones was demonstrated with GDH from beef, chicken, and rat liver, and rat testis, kidney and heart.

A report on these studies by Drs. Yielding and Tomkins appeared in the Proceedings of the National Academy of Sciences.

New studies help explain how genes control cell

Today, one of the most fundamental problems in biology is the manner in which genes determine and control biochemical processes in cells. Basic studies of this control mechanism, which suggest that genes are turned on and off and may explain how this is done, have been reported by scientists at the National Institute of Arthritis and Metabolic Diseases.

Within the past few years, support has been gathered for the hypothesis that genes determine the metabolic pattern in an organism by determining the structure of enzymes, that is, by ordering the sequence of the amino acid building blocks in enzymes. This hypothesis does not account for the fact that some cells of an organism produce enzymes which other cells do not, even though all the cells have the same chromosomes and presumably the same genes. One possible explanation of this is that a mechanism exists for turning genes "off" or "on" and allowing differentiation among the cells.

Dr. Bruce Ames and Miss B. Garry, of the Laboratory of Biochemistry and Metabolism, have approached this problem of genetic control through a study of six of the thousands of enzymes in bacterial cells. These specific enzymes are synthesized by the cell in order to produce histidine, an essential amino acid, and each enzyme catalyzes one step of a multistep process, or metabolic pathway, the end product of which is histidine.

The NIAMD studies have shown that in *Salmonella* bacteria a feedback mechanism regulates the synthesis of the series of enzymes of histidine biosynthesis; the rate of enzyme synthesis slows down as the histidine pool increases. The significant aspects of the finding is that the rates of synthesis of each of the enzymes in the series of enzymes involved in this particular metabolic pathway were repressed to the same extent by histidine. (Other investigators have found that the rate of a single enzyme's synthesis will vary with the size of the pool of the end product, an occurrence called enzyme repression, but this is the first demonstration that a group of enzymes may respond in unison.) The phenomenon has been named "coordinate repression" by the Institute scientists and occurs regardless of the amount or even of the presence of the individual enzyme substrates available in the cell. The NIAMD scientists reported their findings in part in the Proceedings of the National Academy of Sciences recently, and additional aspects of the work will appear in the Journal of General Microbiology (in press).

This new observation is of interest in view of the genetic analysis of various histidine mutant strains of *Salmonella* bacteria. Dr. P. Hartman of Johns Hopkins University has isolated a series of different mutants of *Salmonella* that all require histidine for growth. Each mutant is damaged in one of the genes involved in making an enzyme required for histidine biosynthesis. These genes have been mapped on the *Salmonella* chromosome by Hartman and shown to be in a cluster. The investigations of the NIAMD scientists have shown that each type of mutant Hartman isolated is missing a different enzyme of the biosynthetic pathway. The genes could be associated with the enzymes they control. Hartman's genetic map in conjunction with the NIAMD biochemical studies has revealed the startling fact that the linear order of the genes on the chromosome corresponds to the sequence of the enzymes they control in the biosynthetic pathway.

In view of these two sets of observations, an attractive hypothesis, though one for which direct proof is lacking, is that perhaps the feedback mechanism for regulating histidine production operates at the gene level, and that in some way histidine can functionally "turn off" that length or section of the chromosome containing the genes of the histidine enzymes. Therefore, when the synthesis of the necessary enzymes stops, the production of histidine would stop. The controlling factor may be histidine itself, or a histidine-nucleic acid repressor which has a specific affinity for the histidine section of the chromosome.

Although *Salmonella* exhibits this orderly clustering of genes, it is not found in *Neurospora* or in yeast. The histidine genes in these organisms are scattered on the chromosome, and the investigators are studying them in more detail.

The basic NIAMD research involved in these studies provides a fuller understanding of how genetic information controls biological activity, regulating normal biochemical processes in health and, where enzymatic defects or omissions occur, apparently contributing to or causing biochemical derangements in molecular or metabolic diseases.

Abnormal hemoglobins show effects of genetic mutations

Institute scientists are studying the physical-chemical structure of abnormal hemoglobins to learn more about the effects of genetic mutations on protein synthesis. The studies have shown that the synthesis of the hemoglobin molecule is not controlled by a single gene, but rather that two "halves" of a molecule are synthesized separately—under the control of separate genes—and then joined together to form the complete molecule.

Within recent years it has become apparent that various metabolic disorders in man are associated with the inherited absence or decrease of a particular enzymatic activity. Phenylketonuria, galactosemia and alcaptonuria are all examples of hereditary disorders in which specific enzymes are either lacking or deficient. One possible mechanism for this apparent inhibition of activity is that a mutant gene has caused the production of a structurally abnormal enzyme. This concept of structural abnormality, however, is difficult to test directly, since it is rarely possible to obtain enzymes, especially human enzymes, in adequate purity and quantity for chemical and physical characterization.

One approach to this problem is to study other human proteins, even though they are not classified as enzymes, since the concepts concerning genetic control of protein synthesis apply to these other proteins as well as to enzymes. This is the approach that is being utilized by Dr. Harvey Itano and Elizabeth Robinson, of the Laboratory of Pathology and Histochemistry, in studies of the various types of human hemoglobin. These proteins (the hemoglobins) can be obtained in large quantity and in numerous genetically abnormal forms—hemoglobin S, C, etc.—and provide an extremely useful system for studying protein synthesis and structure.

The NIAMD study has shown that when hemoglobin molecules are placed in an acid medium they will dissociate into two unlike subunits. The molecules are composed of two pairs of amino acid chains, designated alpha chains and beta chains, and in an acid medium the molecules will split asymmetrically, that is, into two alpha chains and two beta chains. When the medium is neutralized, the two unlike "halves" of the molecule recombine to form the complete molecule.

(Normal hemoglobin has two identical alpha chains and two identical beta chains. This is also true of the abnormal hemoglobins, but in them there is an alteration in the amino acid sequence, either of both alpha chains or of both beta chains. As yet no hemoglobins have been found that have alterations in their alpha chains and their beta chains, except in a rare situation in which a person has inherited both a hemoglobin abnormal in the alpha chain and a hemoglobin abnormal in the beta chain.)

The NIAMD scientists have found that all the various types of hemoglobin will undergo dissociation into half molecules and will then recombine not only with their own complementary halves but also with the complementary halves of other types. This phenomenon thus makes it possible to determine where the alteration exists in a hemoglobin of unknown structure. The unknown hemoglobin is mixed with one whose structure is known, and by analyzing the resultant combinations it is possible to determine in what chains, alpha or beta, the unknown is defective. This technique of asymetric recombination has now been used to study many of the abnormal hemoglobins and has clarified the nature of their defects. Recently, the investigators reported in Nature that the phenomenon will take place in an alkaline medium as well as an acid one.

One of the most significant aspects of the NIAMD research is its demonstration that the synthesis of the entire hemoglobin molecule is not controlled by a single gene. Evidently, a separate gene controls the synthesis of each pair of chains, and after the two pairs are synthesized separately they join together to form the complete protein molecule. The hemoglobin studies are thus providing important information on protein synthesis and on the effect of mutations on protein structure.

Taste test indicates inherited traits

A taste test is being used by Dr. Baruch S. Blumberg, of the Institutes program on geographic medicine and genetics, to study one of the many inherited biochemical variations—polymorphisms—that exist among humans. The test employs the compound phenylthiocarbamide (PTC) which certain individuals can taste and others cannot. Since the tasting trait is believed to be genetically determined, the test provides a way to determine the presence or absence of a single gene in the population.

Many such polymorphisms exist in both animals and man, such as unusual types of human hemoglobin, certain synthesized metabolites in the body, and variations that are found among serum hemoglobin binding proteins taken from different individuals. Dr. Blumberg's interest in these biochemical variations stem from the fact that although they are apparently harmless in themselves, they may be affecting an individual's susceptibility to various diseases.

The PTC polymorphism was first reported in 1932, shortly after the compound was synthesized by a Dupont chemist, when family studies of the phenomenon indicated that the trait was a genetically determined one, tasters being dominant for the gene and nontasters being recessive for it. Since then the ratio of tasters to nontasters has been determined in many populations by various investigators. The most recent study was made by Dr. Blumberg in an Alaskan Eskimo population and helps to clarify the worldwide distribution of the tasting trait. The study was made in collaboration with Dr. A. C. Allison of the National Institute of Medical Research, London, and was reported by Drs. Allison and Blumberg in the journal Human Biology.

For many years after its discovery the PTC polymorphism was thought to be only another biochemical oddity until it was discovered that certain other compounds could also be tasted by PTC tasters but not by nontasters. The interesting observation was made that in the chemical structure of all of these compounds there was a characteristic thiourea grouping of nitrogen, carbon, and sulfur which accounted for the tasting phenomenon. This same thiourea grouping is present in a large series of antithyroid substances and known goitrogens, and several studies by other investigators indicate that nontasters may be more susceptible to certain kinds of goiter than are the tasters. The possibility exists than there is some relationship between the PTC tasting polymorphism and the occurrenceo of thyroid disease and is being further explored.

In the Eskimo study, Dr. Blumberg found that the frequency of nontasters was relatively high, 26 percent. This frequency is the same as that found in Western Europeans and comparable to the one existing in the white American population. It is in sharp contrast, however, to the very low frequencies found in American Indians, and the difference is in keeping with many other genetically controlled ones between American Indians and Eskimos which make it improbable that the two populations are related racially.

Further studies of these polymorphisms by the NIAMD scientist may provide important information about the genetic variations that exist among people and populations, and how these variations may influence health and disease.

Study suggests haptoglobins are related to disease

A geographic study of inherited serum proteins called haptoglobins suggests that there may be a relationship between these genetic characteristics and human disease. The study is headed by Dr. B. S. Blumberg of the program on geographic medicine and genetics, National Institute of Arthritis and Metabolic Diseases, NIAMD, and Dr. A. C. Allison of the British National Institute for Medical Research.

The haptoglobins are a family of serum proteins which bind hemoglobin. Although the presence in the blood of three major inherited forms of these proteins has been known for several years, Drs. Blumberg and Allison have now found four additional phenotypes including one in which no haptoglobins are detectable.

In any one individual the pattern of serum haptoglobins is controlled by two genes, termed haptoglobin ^{1} and haptoglobin,^{2} which are not sex linked and are fully expressed in the heterozygote. (Homozygous individuals possess only one type of haptoglobin gene; heterozygous individuals possess both types and they have a more varied pattern of serum haptoglobin.)

The investigators have "mapped" the distribution of haptoglobins and the frequency of the haptoglobin genes in various populations throughout the world. They have found that the haptoglobin ^{1} gene tends to be more common in tropical regions in North and South American and Africa, but not in Asia. Dr. Blumberg and Allison believe that the distribution of these various forms of haptoglobins in different human populations may bear some relationship to disease susceptibility. Studies on the haptoglobins suggest that they may be important in the nutrition of some populations since the absence of haptoglobins results in a loss of hemoglobin in the urine. In regions where iron deficiency is endemic this loss could be a contributing factor in anemia. The scientists have also confirmed previous findings that the concentration of haptoglobins rises in different diseases—in rheumatoid arthritis, for example, and a number of other acute and chronic inflammatory diseases.

The investigators are now attempting to isolate the different haptoglobin types and to break down their components biochemically in an effort to determine the differences and similarities among types. Many aspects of this study have been reported in the scientific literature. One of the more recent publications appeared in the Annals of Human Genetics.

Blood transfusions made safer for newborn infants

Grantees of the National Institute of Arthritis and Metabolic Diseases and the National Heart Institute have found that the mortality rate from exchange transfusions can be greatly reduced by using fresh blood treated with the anticoagulant heparin in place of stored blood that has been treated with sodium citrate to prevent clotting. In a long-term study of 152 exchanges, performed in newborn infants with Rh incompatibility and other hemolytic diseases, the use of heparinized blood resulted in a mortality rate of 7.8 percent; when seven infants with hydrops, a condition from which survival is very rare, were excluded, the mortality rate became 1.8 percent. These rates are in striking contrast to the 13 percent reported earlier by other investigators using citrated blood.

Citrated stored blood has been implicated as the cause of many of the untoward reactions that may occur as a result of exchange transfusions in the newborn. These include convulsions, heart block, generalized irritability, and even death. The enfused citrate causes a reduction in the level of calcium in the serum and spinal fluid, and the subnormal calcium levels then lead to cardiovascular irregularities and to muscle spasms (tetany). Previous reports, although limited in number, have indicated that these and other harmful effects can be circumvented by using fresh heparinized whole blood, and the present study was conducted to determine the value of heparinized blood in a large number of exchange transfusions.

All the exchanges were performed at the University of Minnesota and Minneapolis General Hospitals during the period 1945–59. Of the total number of infants transfused, 130 were treated for Rh sensitization, 12 for ABO incompatibility, and 10 for hyperbilirubinemia (excessive bile pigment in the blood). The procedure was done in the standard way and in almost all cases through the umbilical vein. Tendency toward hemorrhage was easily controlled by subsequent injection of protamine sulfate which counteracted the anticlotting effects of the heparin in the transfused blood. Normal clotting time was restored within 15 minutes.

In summarizing their results, the grantees reported that in addition to the lowered mortality, it was of importance that no deaths occurred during the exchange transfusion, in contrast to the reported instances of cardiac arrest that have occurred during transfusion of citrated blood. Further, there was no evidence of irritability and tetany as may be observed when citrate is used.

"When these advantages and the data in this study are reviewed, it is seen that the use of heparinized blood with proper care and protamine sulfate, can be utilized in the care of erythroblastotic infants to excellent advantage without the hazards associated with other anticoagulants," the investigators concluded.

The study was reported by Drs. Herschel P. Bently, Jr., Newell R. Ziegler and William Krivit, of the University of Minnesota, in the AMA Journal of Diseases of Children.

Rare type of blood antibody discovered

From studies of a surgical patient of the National Heart Institute who developed a severe bleeding tendency 1 week after operation, hematologists of the National Institute of Arthritis and Metabolic Diseases have found that there are two distinctly different types of human blood platelets, a common type and a rarer form. Individuals with the rarer form may develop antibodies against the common type following transfusion, and under certain circumstances as a result of this antibody a patient may destroy his own platelets. The study also provides a clear demonstration that different platelet types exist which are unrelated to red cell types. The significance of this finding with respect to the safety of blood transfusion is not yet fully known.

The discovery of the unusual type of antibody was made by Dr. Raphael Shulman and associates of NIAM's Metabolic Disease Branch, and stemmed from blood studies of a patient who developed uncontrollable internal and external bleeding 1 week after successful heart surgery on the clinical service of the National Heart Institute. At the time she was bleeding, blood studies revealed that all her blood platelets were gone, and on further study it was found that her blood contained an extremely high level of a circulating antibody which reacted with normal platelets and had presumably destroyed all the platelets in her blood. Because her condition was critical an exchange transfusion was carried out to remove the antiplatelet antibody. Within a 16-hour period, during which 90 percent of the patient's blood volume was replaced, all hemorrhage was stopped, and within several days thereafter her platelet count had returned to normal.

It was after the patient recovered, however, that Dr. Shulman made the peculiar finding which suggested that the woman might have an unusual type of platelet. He took a fresh sample of blood from the patient (a sample containing her newly restored platelets) and mixed it with some of the antibody-containing blood that had been flushed out during the exchange transfusion. Since the antibody was active against normal platelets, it was assumed that it would also be active against the patient's platelets, but no reaction took place. This finding was corroborated in a second patient (hospitalized at Faulkner Hospital in Boston) with the same clinical history of hemorrhage 1 week after transfusion; that is, the platelets of both patients after recovery would not react with the antibody which was present in their blood at the time they were bleeding. This could have been due to some agent in the patients' blood which blocked the attachment of antibody or to the fact that the patients' platelets were different from usual normal platelets.

Geneologic studies by the NIAMD investigators of platelet type in 35 members (covering 4 generations) of the family of one of the patients as well as a general population survey of platelets from 100 randomly selected individuals indicated that the patients indeed had an unusual form of platelets and that this form of platelets is inherited as a recessive trait. Platelet typing was done using the original antibody from the patients. The unusual form of platelet was not as rare as had been expected for 2 percent of the population proved to have it, indicating that the chances of the usual form of platelets being transfused into an individual with the unusual form is approximately 1 in 50. It is evident that reactions are not caused every time this is done, for it was found that a patient with the rare type could receive as many as 17 transfusions with the common type without provoking antibody. In addition, there are only two other cases in the medical literature which might have had the same complication.

The NIAMD hematologic studies suggest that in order to develop an antibody and have the antibody destroy an individual's own platelets, the donor of the common type of platelets might have to be unusual also. It appears that some individuals with the common type platelet may very rarely have some of the antigen substance from their platelets free in their blood. This free substance transfused into a patient with the uncommon form of platelet may not only be necessary in order to provoke antibodies in the recipient but also may be necessary to coat the recipient's platelets and thus permit antibody to react, leading to lysis of platelets and possible severe hemorrhage.

The studies were reported to the American Society for Clinical Investigations by Drs. N. R. Shulman, R. Aster, A. Leitner, and M. Hiller.

Blood studies provide new facts about a vital process

One of the most vital of all physiological processes is the binding of oxygen by hemoglobin, a process which enables red blood cells to transport oxygen throughout the circulation. Basic studies of human hemoglobin by Dr. Makio Murayama of the Institute's Laboratory of Pathology and Histochemistry have now provided valuable new information about the mechanisms of this complex binding process. The studies were reported in the Journal of Biological Chemistry.

The objective of the research was to study the way in which hemoglobin binds heavy metals, such as mercury, arsenic and copper. The binding takes place at eight heavy metal-binding sites on each of the hemoglobin molecules, and the mechanisms of this type of binding are believed to be analogous to those of oxygen binding, which takes place at four other binding sites on the hemoglobin molecule. Thus, a full understanding of heavy metal binding can help to explain the oxygenation process. Heavy metal binding and oxygen binding can be looked upon as two sides of the same coin, since the binding sites are all close together in the molecule and influence one another.

Dr. Murayama's study of the eight heavy metal-binding sites has revealed that a cooperative interaction takes place among them. That is, once the first heavy metal ion attaches to a binding site, it becomes progressively easier for succeeding metal ions to attach to the remaining sites. The binding sites are inside the molecule rather than on its surface, and the process can be visualized as a "wedging apart" of the hemoglobin molecule. As the wedging increases it becomes easier for additional metal ions to get inside the hemoglobin molecule, attach to its binding sites, and increase the wedging effect. This type of cooperative interaction is also known to exist at the four oxygen-binding sites. At the heavy metal sites the interactions are known as mercapto-mercapto interactions (mercury-capturing interactions), and at the oxygen sites they are known as heme-heme interactions.

The NIAMD scientist has been able to determine the physical "constants" that govern the mercapto-mercapto interactions and, for the first time, measure the degree of interaction. Such measurements provide a most useful adjunct to studies of oxygenation mechanisms.

The present study also suggests an interesting approach to the treatment of sickle cell disease, a disorder caused by an abnormal type of hemoglobin known as S hemoglobin. Molecules of S hemoglobin have an abnormal shape; when they are not carrying oxygen they appear to "stack up" inside the red blood cell, and the cell becomes twisted into its characteristic sickle shape. Such sickle-shaped cells seriously impair blood flow in the capillary network and account for the pathology of the disease. The apparent stacking does not occur as long as S hemoglobin molecules are wedged apart, either by oxygen molecules or by heavy metal ions, so that sickling could be prevented if heavy metals were kept bound to the hemoglobin. Unfortunately, the heavy metals are too toxic for this purpose. What is needed, therefore, is some innocuous material that would attach to the heavy metal-binding sites and keep the S hemoglobin molecule wedged apart. Studies are being continued in an attempt to find a material that might accomplish this purpose.

Gamma globulin effective against postburn infections

Studies of burned children in Lima, Peru, have shown that injections of gamma globulin may reduce the incidence of deadly postburn infections by nearly one-half, a National Institute of Arthritis and Metabolic Diseases' scientist reported to the First International Congress on Research in Burns. Dr. Nicholas A. Kefalides of the Laboratory of Pharmacology and Toxicology reported the successful results of a continuing study of burns and their treatment which has been carried out in both NIAMD laboratories and the Children's Hospital in Lima.

The gamma globulin treatment was developed to counteract the overwhelming infection usually caused by *Pseudomonas aeruginosa*, a micro-organism that is resistant to all commonly used antibiotics. In instances of severe burns the primary cause of death is burn shock; however, many times patients survive the shock period only to succumb to the bacterial infection within several days.

Earlier NIAMD animal studies by Drs. R. C. Millican and S. Rosenthal indicated the value of gamma globulin, the blood serum fraction containing antibiotics, in combating the postburn infection. Clinical trials of gamma globulin therapy began in 1957 on burn victims at the Lima hospital and the value of the treatment has now been established in over 100 cases.

In a control group of 111, the incidence of septicemia (generalized blood infection) was 41 percent. In the 104 gamma globulin patients the septicemia was 21 percent. Patients received approximately 60 milliliters of gamma globulin. Treatment was most effective in children under 4 years old with burns under 25 percent of the body area. In older children, although the gamma globulin treatment significantly lowered the incidence of septicemia, it had considerably less effect on total late mortality.

"The results indicate that antiobiotic prophylaxis does little to prevent wound infection or septicemia, while gamma globulin prophylaxis significantly reduced septicemia and mortality in young children," Dr. Kefalides reported.

Physical biologists uncover new facts about photosynthesis

Studies by physical biologists at the National Institute of Arthritis and Metabolic Diseases are providing important new facts about photosynthesis. Of considerable interest is the structure of the chloroplasts, the small green bodies in higher plants and green algae which contain chlorophyll, the major photosynthetic pigment. In the section on photobiology, headed by Dr. F. S. Brackett, NIAMD scientists are developing new techniques and instruments to uncover how the chloroplasts capture the energy of sunlight and use it to product organic compounds from carbon dioxide and water.

Using a technique known as absorption microscopy, Drs. R. A. Olson and C. L. Greenblatt, and E. K. Engel, have been able to confirm—by light microscopy—what had been previously suggested by electron microscope studies. This was that chlorophyll exists in a number of layers inside the living chloroplasts. This lamellar structure, a "sandwiching" of a layer of single molecules of chlorophyll with layers of protein and lipid, is believed to be an aspect of the essential structural characteristics of the chloroplasts which enables them to convert light energy to chemical energy. The work was reported in The Journal and Biophysical and Biochemical Cytology.

Dr. Olson and his NIAMD associates have also constructed a device to measure the emission spectra of Chlorella, a simple chlorophyll-containing alga. These plants, like all photosynthetic ones, fluoresce when excited by light of particular wavelengths (in this case 4358A), and the characteristics of this emitted light help to identify the metabolic changes taking place in the cells. The new instrument, known as a rapid scanning microspectrofluorimeter, can scan the spectra of the emitted light as rapidly as once a second. It will be described in detail in the August issue of The Review of Scientific Instruments.

These NIAMD studies of photosynthesis, only a small part of the Institute's total research in physical biology, have produced three valuable results. First, the studies provide a means for studying energy transfer in a biological system where the input energy (light) can be measured exactly; second, they provide a convenient system for studying the synthesis of porphyrin compounds, compounds which include, in addition to chlorophyll, the heme in hemoglobin as well as the various cytochromes that play a vital role in cell metabolism; and third, the studies are leading to the development of the very specialized tools needed for biophysical research. In the near future these same tools may find valuable application to many problems of human cellular metabolism.

Advanced electronic technique used to study atomic structure

Physical biologists at the National Institute of Arthritis and Metabolic Diseases have used an advanced electronic technique known as nuclear magnetic resonance to study the atomic structure of porphyrins, complex molecules found in hemoglobin, chorophyll and other important biological materials.

The porphyrins are pigments which occur throughout the plant and animal world. They form the base of chlorophyll in plants and hemoglobin in man and readily combine with metals such as iron and magnesium. The porphyrins are of fundamental importance to many oxidation-reduction reactions in the body and are also known to affect radiation sensitivity. Persons afflicted with one of the forms of porphyria, a rare disorder of poryhyrin metabolism, are sensitive to light and must avoid direct exposure to the sun. In radiation research certain porphyrin compounds have been used to protect animals against lethal doses of radiation.

The NIAMD study was done to learn more about the atomic structure of these important molecules and utilized nuclear magnetic resonance (NMR) equipment. The study was reported by Dr. Edwin D. Becker and Robert B. Bradley of NIAMD's Laboratory of Physical Biology in the Journal of Chemical Physics.

The NMR technique of the physical biologists makes it possible to determine the presence or absence of certain functional groups (OH, NH, etc.) in a molecule and to determine the relative positions of these groups, thus giving a three-dimensional picture of molecular structure. The test substance is placed in a strong magnetic field and bombarded with radio waves which can be varied in frequency. Once in the magnetic field, the molecules of the sample substance absorb radio waves of certain frequencies, the particular frequencies being determined by the atomic structure of the molecule. By noting what frequencies are absorbed, the investigators can determine what atomic particles are present and how they are arranged.

NMR analysis of several nonmetallic porphyrin compounds revealed that their NMR spectra had considerably different values from those that had been expected. The NIAMD scientists found that the differences could be accounted for in large part by the presence of a "ring current" around the porphyrin molecule. The molecule has a ringlike structure and the current is due to flow of electrons around the periphery of the molecule. Such a current would produce a small magnetic field that would interact with the larger field of the NMR equipment, and this would account for the unexpected results.

The finding is of considerable interest to other NMR spectroscopists for it will explain what would otherwise be confusing experimental results. Additionally, the NIAMD study has indicated that some unknown structural factor may also be involved, suggesting that the presently accepted "model" of the porphyrin molecule is inadequate. Further studies to clarify this point will be done on samples of metal-containing porphyrins.

The porphyrin samples used in the study were provided by Dr. Cecil J. Watson, professor of medicine at the University of Minnesota Medical School, who is chairman of NIAMID's Board of Scientific Counselors. Dr. Watson has specialized for many years in the study of porphyria and spent several months at the Institute last year as a visiting scientist.

PROGRAM DEVELOPMENT

World Nutrition Congress draws 2,000 scientists to Washington

Over 2,000 nutrition scientists participated in the week-long Fifth International Congress on Nutrition which was held in Washington, D.C., and opened by President Eisenhower. During the Congress, the first to be held in the United States, experts from 65 nations reported on nutritional progress throughout the world and discussed the food problems that still exist in many areas. Two of the interesting highlights of the international meeting were reports that underproduction of food, not overpopulation, will be the major nutritional problem facing the world for the next 40 years; and that in the United States the worst nutritional problem is overeating.

A number of special panel discussions were held on such subjects as the evaluation of nutritional status in man, nutrition in maternal and infant feeding, the effects of processing and additives on foods, and the new possibilities in nutrition research. In addition, there were many individual study sections. These covered the whole spectrum of nutrition studies from proteins and amino acids, to the effect of bile acids on plasma cholesterol.

As well as the great number of important basic scientific studies that were reported to the Congress, there were also some of immediate practical value, such as new and effective means of preventing protein deficiency on a populationwide scale. This is one of the most acute nutrition problems existing in some of the underdeveloped areas of the world; in Africa and Central and South America it accounts for the high incidence of the disease known as kwashiorkor, a protein malnutrition syndrome which often leads to death and occurs in children who are fed an almost exclusive starch diet. One successful solution to this problem has been developed by the Institute of Nutrition for Central America and Panama (INCAP). Under grants from the National Institute of Arthritis and Metabolic Diseases, INCAP scientists have developed a vegetable protein formula which has a well-balanced amino acid profile and, most importantly, is based on locally produced agricultural products. The special high protein diet is called Incaparina and contains 38 percent cottonseed meal, 29 percent cornmeal, 29 percent sorghum meal, 3 percent yeast, and 1 percent calcium carbonate. The diet has proven extremely valuable in preventing and treating kwashiorkor, and this classic achievement by INCAP points the way to similar economically feasible solutions to the problem of protein deficiency in other undernourished regions of the world.

Staff members of the National Institute of Arthritis and Metabolic Diseases (NIAMD) presented eight papers and participated in committe and other functions of the Congress. A total of 18 papers were given by the National Institutes of Health staff, with the largest number 4, devoted to research with germ-free animals.

The congress was sponsored by the International Union of Nutritional Sciences, the American Institute of Nutrition, and the National Academy of Sciences—National Research Council. It was supported, in part, by the NIAMD, the National Cancer Institute, and the National Institute of Dental Research.

Natural history of diabetes subject of large new study

The first large-scale, carefully controlled and long-term study of the natural history of diabetes is now in its pilot stage at seven research centers located throughout the country. Under grants from the National Institute of Arthritis and Metabolic Diseases (NIAMD), the new university group diabetes study will investigate the incidence and severity of late diabetic complications such as retinopathy, atherosclerosis, kidney and nervous system disorders, in large groups of reasonably controlled patients treated in various ways. Such diabetic complications have long been of great concern to the medical profession; diabetes is, for example, numerically the greatest cause of blindness in the United States.

The study, originally conceived as an investigation of the effects of oral hypoglycemic agents (drugs which reduce blood sugar levels) on diabetes, has been designed to determine the rate of development and severity of late diabetic complications and to determine if this rate is in any way affected by several therapeutic measures involved in the study on a long-term basis.

The therapeutic measures being used to control diabetes are: (1) Special diet, (2) special diet plus the oral drug tolbutamid, (3) special diet plus insulin given in dosage to maintain good chemical control of blood sugar levels, (4) special diet plus a fixed dosage of insulin administered on the basis of body weight.

The first year of the NIAMD-sponsored study is regarded as a trial run and patients selected for the pilot stage will be disqualified when the full-scale investigation gets underway early in fiscal year 1962. Approximately 700 patients, 100 at each center, will be included in the study, and the patients will be selected from those diabetics whose disorder has been diagnosed within 6 months prior to inclusion in the study, and who have had no previous therapy. In addition, their disease must be controllable by diet alone and they must have a life expectancy of at least 5 years. Patients are subjected to batteries of tests at the centers on a repeating basis. After careful instruction, they will run certain of their own tests, administer their own drugs, check their own diet and record all data in individual diaries.

Seven principal investigators, an emient epidemiologist and some 25 of their associates now compose the group. These investigators are: Dr. Max Miller (chairman), University Hospital, Western Reserve University, Cleveland; Dr. Christian R. Klimt (group epidemiologist and chief of the coordination center), School of Public Health. University of Minnesota; Dr. Richard A. Field, Massachusetts General Hospital, Boston; Dr. Frederick C. Goetz, Medical School, University of Minnesota; Dr. Martin G. Goldner, Jewish Chronic Diseases Hospital, Brooklyn, N.Y.; Dr. Charles A. Jones, Williamson Memorial Medical Center, Williamson, W. Va.; Dr. Harvey C. Knowles, Jr., University of Cincinnati, Department of Internal Medicine, Cincinnati General Hospital, Ohio; and Dr. Thaddeus E. Prout, School of Medicine, Johns Hopkins University, Baltimore. Dr. James W. Pratt, NIAMD, serves as liaison officer to the group.

In addition to NIAMD funds, the group receives support from the individual investigators' own institutions. The Upjohn Co., Eli Lilly & Co., and the Ames Co., Inc., have agreed to provide drugs and products for the study without having a voice in the management of the study. The trials were approved by the NIAMD Advisory Council for a period of 7 years and are forecast to run for a minimum of 10. If successful, the study could become a prototype for large-scale cooperative clinical trials in other disorders.

Tuesday, April 11, 1961.

GRANTS FOR CONSTRUCTION OF HEALTH RESEARCH FACILITIES

WITNESSES

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. FRANCIS L. SCHMEHL, CHIEF, HEALTH RESEARCH FACILITIES
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities: Grants for construction and equipment (total costs—obligations) (object class 41)	30,039	30,001	30,000
Financing:			
Unobligated balance brought forward	−40	−1	
Unobligated balance carried forward	1		
New obligational authority (appropriation)	30,000	30,000	30,000

Mr. Fogarty. The committee will come to order.

Who is going to make the opening statement on the grants for construction of health research facilities?

Dr. Shannon. Dr. Schmehl, Chief of the Health Research Facilities Branch, Division of Research Grants, will make the opening statement.

Dr. Schmehl. Thank you, Mr. Fogarty. It is a pleasure to read this opening statement.

General Statement

Mr. Chairman and members of the committee, a request in the amount of $30 million is submitted under this appropriation for 1962. These funds were authorized under the initial basic legislation, Public Law 84–835, which added title VII to the Public Health Service Act. It provides for Federal assistance in the construction and/or equipping of facilities for research in the sciences related to health. This act was extended for an additional 3-year period (Public Law 85–777) in August 1958, thus providing an authorization of up to $30 million a year for 1960, 1961, and 1962. Public Health Service grants, under this title, are awarded to non-Federal public and private nonprofit institutions, competent to engage in the type of research for which the facility is to be constructed, on a matching basis, with the Federal share not to exceed 50 percent of the costs of the research portion of such construction. All awards must first be recommended for approval by the National Advisory Council on Health Research Facilities, established under the law. This program is administered by the Division of Research Grants of the National Institutes of Health.

Appropriations of $150 million have been made by the Congress for the first 5 years (1957 through 1961).

Annual reports, in accordance with the law, have been submitted to the President and transmitted to the Congress. These have been printed as public documents as follows: House Documents 21 and 324 of the 85th Congress and House Documents 73 and 344 of the 86th Congress. The fifth and current annual report has been referred to the Congress on March 14, 1961, and has been ordered printed as House Document 110, 87th Congress, 1st session. And if I may depart from the prepared text, it is a pleasure to inform you this report has been issued from the Government Printing Office and is available.

GRANTS AWARDED

Federal funds in the amount of $321,181,090 have been requested since the inception of this program by eligible applicants for the purpose outlined in the Health Research Facilities Act. These requests have been thoroughly documented in a total of 1,126 new, revised, and supplemental applications from institutions doing health related research—public and private nonprofit schools of medicine, dentistry, osteopathy, and public health; hospitals, universities, and other research institutions. From the $150 million appropriated for the first 5 program years, 755 grants have been awarded to 320 institutions, in 47 States, the District of Columbia, and Puerto Rico, in the amount of $149,921,407.

Grants for research facilities to medical schools total $78,569,909; dental schools $2,676,281; osteopathy $112,569; and schools of public health $3,123,105. Other health related school areas such as veterinary medicine, pharmacy, chemistry and biological sciences have received research facilities grants totaling $31,583,145 and public and private institutions, other than schools, engaged in research have received awards valued at $33,856,398. Of the total allocated, non-Federal public institutions have received 44 percent of these Federal funds and private nonprofit institutions 56 percent.

CONSTRUCTION PROGRESS

This past year has shown considerable progress in construction, completion, and utilization of new, remodeled, and renovated facilities. As of December 1, 1960, 238 projects had been completed with a Federal investment of $31,693,011. This represents a dollar value almost double that shown for completed grants reported in the fourth annual report of the Surgeon General, which summarizes the activities of this program through December 31. 1959, and which was transmitted to the Congress on February 17, 1960. Since many of the larger research facilities were completed and put into use during calender year 1960, the total number of completed projects increased by a little more than 60 precent.

As of March 10, 1961, 265 projects have been completed with a Federal investment of $37,809,936. In addition, there are 187 projects under contract, many of which are nearing completion, and 133 projects for which final contract commitments have not as yet been made. This number does not include supplementary grants for movable equipment.

CURRENT STATUS

As of March 10, 1961, the program demand was as follows:

1. Approved projects recommended by Council and awaiting payment	$22, 112, 444
2. Pending: New and deferred applications awaiting Council action (126)	48, 714, 621
3. Intentions to submit applications (93)	33, 652, 846
Total	104, 479, 911

That concludes the formal report.

Mr. Fogarty. Does that mean you could use $104 million in 1962?

Dr. Schmehl. It means we could use a substantial portion of that, Mr. Fogarty.

Mr. Fogarty. How much?

Dr. Schmehl. I would say 80 percent of that.

Mr. Fogarty. We can't do much about it because the authorization only——

Dr. Schmehl. Yes, I realize that. This represents my estimation of the extent to which Council would use that $104 million.

Mr. Fogarty. With these figures, do you think that the new legislation that is being proposed to raise this to $50 million a year would be enough?

Dr. Schmehl. I think it would go a long way, Mr. Fogarty.

Mr. Fogarty. To go all of the way, how much do you think we ought to authorize per year?

Dr. Schmehl. Well, I believe it is a question of time, also. Fifty million for 3 years——

Mr. Fogarty. I don't want to beat all around the bush with you now. Give me the amount you think could be used per year.

Dr. Schmehl. Well, if I can pull one out of the hat, I would say $65 million a year.

Mr. Fogarty. Is that conservative?

Dr. Schmehl. I would say that was a realistic estimate.

Mr. Fogarty. Mr. Marshall?

Mr. Marshall. No questions.

Mr. Fogarty. Thank you very much.

What is next?

Dr. Shannon. The Special Foreign Currency Program. We asked Mr. Murtaugh to present this program since he has been the one involved both in this country and overseas and we thought it would be more suitable for him to present it.

TUESDAY, APRIL 11, 1961.

SCIENTIFIC ACTIVITIES OVERSEAS (SPECIAL FOREIGN CURRENCY PROGRAM)

WITNESSES

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
SCOTT ADAMS, DEPUTY DIRECTOR, NATIONAL LIBRARY OF MEDICINE
DR. DAVID SENCER, COMMUNICABLE DISEASE CENTER, ATLANTA, GEORGIA
JOSEPH S. MURTAUGH, CHIEF, OFFICE OF PROGRAM PLANNING, NATIONAL INSTITUTES OF HEALTH
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities: Foreign health research (total costs—obligations) (object class 25)		3,707	10,084
Financing: New obligational authority (appropriation)		3,707	10,084

GENERAL STATEMENT

Mr. MURTAUGH. Mr. Chairman and members of the committee, the opening statement has been submitted for the record.

(The statement referred to follows:)

Mr. Chairman and members of the committee, it is a pleasure for me to appear before you today to present the special foreign currency program of the Public Health Service. This program contains proposals for the support of medical research and other scientific activities through use of foreign currencies by the National Institutes of Health, the Bureau of State Services, and the National Library of Medicine.

Since the National Institutes of Health has had approximately 1 year's experience in developing this program I have been asked to present all of the Public Health Service programs. It is believed that this consolidation of presentation will save time for the committee.

The total request of the Public Health Service for fiscal year 1962 to purchase foreign currencies to finance and conduct scientific activities overseas amounts to $10,084,000, of which $5,717,000 is requested by the National Institutes of Health, $3,700,000 by the Bureau of State Services, and $667,000 by the National Library of Medicine. These oversea programs would support research in seven different countries. The programs of the National Institutes of Health would support medical research with major emphasis on problems related to infectious diseases, nutrition, and problems which can be best investigated utilizing large and diverse population groups as the research subject. The programs of the Bureau of State Services are primarily directed toward communicable diseases, environmental health, and behavioral studies. The programs of the National Library of Medicine are primarily for translations of research publications in medical and related sciences and for the preparation of "critical review" papers, medical dictionaries, directories to research institutions, bibliographies, and other guides designed to improve the ability of American medical scientists to communicate with scientists in other countries. This request would also provide funds to assist in developing plans for a Second International Congress on Medical Librarianship, such funds to be used for international travel incidental to organizing the Congress.

The sum of $3,707,000 was appropriated to the National Institutes of Health for the current fiscal year (1961) to support research activities in eight countries: Brazil, Egypt, India, Indonesia, Israel, Poland, Pakistan, and Yugoslavia. We have made some progress in mounting our programs in these countries. We found it necessary to conduct discussions at the governmental level prior to negotiating individual projects on a scientist-to-scientist basis. These governmental discussions have been conducted in all countries except Brazil and Indonesia. These discussions are planned for Indonesia in connection with another project-negotiating trip and will be conducted in Brazil as soon as we receive word from the State Department that the Public Law 480 sales agreement with Brazil has been completed to permit us to use these funds for medical research. Informal correspondence has been carried on between scientists at the National Institutes of Health and their scientific counterparts in all countries where we have proposed projects for 1961. A team of negotiators are now in Israel and Yugoslavia to develop firm agreements for the conduct of research projects. Plans are currently being developed to conduct final negotiations and specific project agreements in Egypt, Pakistan, and Poland. The program will be carried out as a direct extension of the intramural research programs and interests of the several institutes comprising the National Institutes of Health, Public Health Service. Research projects developed under this program will be carried out under research agreements with collaborating institutions and investigators in the countries involved.

Mr. Fogarty. Your appropriation for 1961 is $3,707,000 and the request for 1962 is $10,084,000.

Mr. Murtaugh. Yes, sir.

Mr. Fogarty. An increase of $6,377,000. Over half of this increase is for the Bureau of State Services.

Mr. Murtaugh. Yes, sir.

Mr. Fogarty. They haven't had any of these funds before?

Mr. Murtaugh. Not previously. This will be the first year.

Environmental Health

Mr. Fogarty. Can you explain in a little more detail what activities are planned with this amount of money for the Bureau of State Services?

Mr. Murtaugh. There is a great deal of interest on the part of both the Communicable Disease Center and the portions of the Bureau of State Services concerned with environmental health in utilizing these funds to carry out cooperative research work with scientists and investigators in the several countries in which these funds are available. This gained particular emphasis from the fact that our preliminary negotiations in Poland indicated the interest of the Polish Ministry of Health and Polish scientists to engage in research work in areas emphasizing the communicable diseases and areas of environmental health. Both of these areas are of interest to the Bureau of State Services.

POLAND

Mr. Fogarty. Tell us just what you are doing in Poland and what you plan to do. Use Poland as an example of the eight countries.

Mr. Murtaugh. In the latter part of October of 1960, a team comprised of a scientist from the National Institutes of Health and an administrator visited Poland. They had discussions with officials of the Polish Ministry of Health, in which the intentions of the National Institutes of Health to propose projects for collaborative research with Polish scientists utilizing Public Law 480 funds was described. The programs discussed involved a study of the encephalitides in Poland and research in cerebrovascular disease. These projects had been proposed by NIH investigators on the basis of their knowledge of interest and opportunities in Poland. These proposals and the general concept of collaborative research arrangements with the PHS were well received by the Ministry of Health. However, the Ministry of Health officials pointed out that these arrangements would have to have the affirmation of the Ministry of Foreign Affairs of the Polish Government before the Ministry of Health and its scientists could enter into such relationships.

Visits were made to the Ministry of Foreign Affairs and the proposals and plans of the National Institutes outlined to the Ministry officials. Again they were well received, but they asked for submission of a formal aide memoire from the U.S. Government setting forth our plans. This was done in the first part of October 1960. No reply was received to this aide memoire until the middle of February of this year. At that time a communication was transmitted by the Polish Government to the American Embassy in Warsaw indicating the acceptance by the Polish Government of the proposals of the National Institutes of Health to carry out this collaborative work in relationship with the Ministry of Health in Poland.

Because of the fact that our earlier discussions indicated the interest of the Polish Government to join in research work in areas beyond that proposed by the National Institutes of Health and the fact that the Bureau of State Services was interested in these areas, it has been felt that we ought to delay further discussions in Poland until it was clear whether or not funds would be available to the Bureau of State Services. If so, we would take further steps to negotiate individual research projects in Poland. This step is contemplated in June or July of this year, that is if the request for these funds is favorably looked upon by the committee.

Mr. FOGARTY. So you won't be doing anything in Poland until the start of the next fiscal year?

Mr. MURTAUGH. Very probably not.

DIFFICULTIES IN NEGOTIATING RESEARCH PROGRAMS

Dr. SHANNON. Might I say, Mr. Fogarty, this is characteristic of all of these programs. It takes, according to our best guess now, no less than about 9 months to complete an agreement. One must go through the various ministries that are concerned with the expenditure of this particular type of money to obtain approval of the appropriate bodies in the country before one can move on to the institution itself to complete the final agreement.

Mr. FOGARTY. I thought we were trying to eliminate a lot of that redtape.

Dr. SHANNON. Mr. Fogarty, all I can say is that in our experience none of it has been eliminated. This is a very long, drawn out negotiation process that has many blocks along the way. I think this is perhaps best pointed up by the fact that despite a good deal of work on our part during the past year, we are yet to have a program in operation. The first programs that will be in operation before the end of this fiscal year are two projects in Israel where we are about to complete negotiations. The problems associated with the use of these funds goes beyond simply setting desirable collaborative objectives. They get into the realm of the finances of the country. These funds in a very real sense, if they are used extensively, constitute an inflation of that country's currency. Because of this these countries are very chary about the development of these programs and must feel assured that the benefits to be derived far outweigh the problems that might be created by the use of the funds.

Mr. Fogarty. You mean to say that these amounts you are talking about now would effect the economy of any country, any of these eight countries?

Dr. Shannon. No, sir. They are quite aware of the fact that these sums as such will not be disruptive to their currency plans, but if this approach were to be rapidly expanded into many areas, then they very well might.

INDIA

In one country, namely, India, where a program is proposed to be undertaken in the aggregate, I believe, Mr. Murtaugh, of a million, two——

Mr. Murtaugh. It is $1.8 million in 1961.

Dr. Shannon. This was a very substantial amount of the total money that India felt could be expended for medical research considering the scientific resources available to them as a nation.

Mr. Fogarty. If there is a country in the world that needs help in that area, it is India.

Dr. Shannon. Yes, sir. We completed our preliminary negotiations there and had arranged for a technical visit to firm up the actual projects with the Indian institutes that would be concerned. This was to take place at about the time that the WHO met in New Delhi. About 2 weeks before the delegation was to take off from this country, we received a cablegram from the Ministry of Health saying that we should hold up the delegation, that the utilization of these funds for these purposes were sufficiently outside the 5-year plan for medical research of India, that their use would have to be confirmed subsequent to cabinet discussions. When these discussions were undertaken or had been completed by the Indian health authorities they looked forward to favorable action and they would then be prepared to receive a delegation.

These sums are not going to be used rapidly. It was actually in anticipation of this difficulty that, as a matter of policy Public Health Service permitted the NIH to proceed with a small program during the initial years to acquire know-how and understanding of the problems. Only in the second year, after some understanding of these problems were had, did they permit the Bureau of State Services to add a second program to the NIH program. Actually, the Bureau of State Services did have a program proposed during the initial year, but as a matter of policy the Public Health Service thought it would be unwise for them to attempt it.

These funds, as they are appropriated, are for total support of a project over a period of 3 to 5 years, so that even though the project takes the better part of a year to establish, funds are available for the completion of the project. It is a disappointment to us that this program has not moved faster, but with a rather extensive commitment in support of research overseas, we feel a positive need to attempt to use these block currencies effectively. We are therefore quite willing to fight through the administrative morass and get these programs underway.

It is predictable that some of the projects presented before this committee will not come into being but the way the funds are derived by the appropriation process, we must propose plans by country. We must have the availability of those funds assured to us before we can undertake the initial negotiations. In the final analysis it will depend upon whether or not we can arrive at an agreement with a particular country within these earmarked funds as to whether or not they will be expended in support of these collaborative research projects. This is truly a massive administrative job out of all proportion to the sums of money expended. We feel once the mechanisms are cleared away and the programs actually are in operation, then their continuation and, if necessary, their extension, will have made this primary effort well worth while. But it takes a massive administrative effort to get the programs underway.

Mr. Fogarty. If you are disappointed, I might say I am doubly disappointed that you haven't made more progress than you have, and there are many other people feel the same way.

Mr. Murtaugh. Might I add a point, sir? In case there might be any misunderstanding, the administrative and operational problems that we have encountered in this program have, in large part, been a result of necessity of reaching these preliminary agreements with the countries involved and have been the result of the delays imposed in the process of these negotiations. We have had excellent assistance and cooperation from the Office of Science Advisors, State Department, and from embassy officials that have worked with us on this program. In most cases our scientific counterparts in the research institutions and ministries of health of the countries we have visited have been quite willing to cooperate, but they have been under the obligations and restrictions imposed upon them by their ministry of finance or ministry of foreign affairs which view these as developments in a larger context.

Mr. Fogarty. How many countries are eligible? Just eight?

Mr. Murtaugh. The funds that are made available to us or indicated to be available are in only seven countries in 1962. These are countries where these currencies are excess to regular U.S. requirements.

LIST OF PROJECTS BY COUNTRIES

Mr. Fogarty. Put a list of the countries in the record and also what kind of projects you hope to activate in 1962.

Mr. Murtaugh. Yes, sir.

Dr. Shannon. This we will be glad to do.

(The material requested follows:)

Department of Health, Education, and Welfare—Public Health Service

National Institutes of Health	$5, 717, 000
Bureau of State Services	3, 700, 000
National Library of Medicine	667, 000
Total	10, 084, 000

National Institutes of Health—Estimates using foreign currency

Country and projects	1961 estimate by project	1962 estimate by project
Brazil:		
1. Schistosomiasis	$85, 000	0
2. Native botanicals	50, 000	0
3. Venoms	25, 000	0
Total, Brazil	160, 000	0
Burma:		
1. Malnutrition and beriberi	0	$315, 000
2. Malaria	0	164, 000
Total, Burma	0	479, 000
Egypt:		
1. Schistosomiasis and trachoma	0	309, 900
2. Schistosoma-bladder cancer	0	154, 300
3. Schistosomiasis	140, 000	194, 300
4. Intestinal helminths	0	194, 300
5. Ophthalmology	0	92, 200
6. Pellagra and anemia	129, 000	0
7. Bladder cancer	18, 000	0
Total, Egypt	287, 000	945, 000
India:		
1. Periodontal disease	0	107, 500
2. Diabetes	0	211, 000
3. Cholera	55, 000	49, 200
4. Tropical Eosinophilia	0	159, 300
5. Amoebiasis	0	252, 200
6. Toxoplasmosis	0	96, 500
7. Virus diseases	0	96, 500
8. Native botanicals	0	24, 000
9. Cardiovascular disease	0	190, 000
10. Cerebral vascular diseases	0	63, 600
11. Central nervous system	0	63, 700
12. Infant development	0	128, 500
13. Malaria	340, 300	0
14. Filariases	281, 900	0
15. Cancer	57, 500	0
16. Epidemiology of cancer	66, 000	0
17. Kwashiorkor	679, 000	0
18. Manganese intoxication	22, 000	0
19. Jatamonsone	33, 000	0
20. Geographic pathology	180, 000	0
21. Vascular diseases	30, 000	0
22. Intracranial epidemiology	37, 300	0
Total, India	1, 782, 000	1, 442, 000
Indonesia:		
1. Mycological investigations	88, 000	0
Total, Indonesia	88, 000	0
Israel:		
1. Toxoplasmosis	0	127, 350
2. Cardiovascular disease	110, 000	106, 850
3. Central nervous system	0	95, 700
4. Ophthalmology	0	156, 200
5. Infant development	0	126, 900
6. Studies of O^{18}	80, 000	0
Total, Israel	190, 000	613, 000
Pakistan:		
1. Diabetes	0	208, 200
2. Cholera	414, 000	413, 800
3. Malnutrition	271, 000	0
Total, Pakistan	685, 000	622, 000

National Intitutes of Health—Estimates using foreign currency—Continued

Country and projects	1961 estimate by project	1962 estimate by project
Poland:		
1. Trichinosis	0	207,750
2. Encephalitides	20,000	62,000
3. Cerebral vascular diseases	95,000	47,000
4. Perinatal diseases	0	157,550
5. Brain-behavior research	0	611,700
Total, Poland	115,000	1,086,000
Yugoslavia:		
1. Pellagra	0	155,900
2. Virus diseases	0	218,200
3. Perinatal diseases	0	155,900
4. Heart disease	400,000	0
Total, Yugoslavia	400,000	530,000
Total	3,707,000	5,717,000

Bureau of State Services—Estimates using foreign currency

Country and projects	1961 estimate by project	1962 estimate by project
India:		
1. Ecology of enterovirus infections in central India	0	$75,000
2. Gonorrhea and pelvic inflammatory disease investigations in Calcutta	0	25,000
3. Investigation by fluorescent tagged antibody technique of the prevalence of gonococcal infection in the female and relation to complications	0	50.000
4. Investigation of the problem of infections with atypical acidfast bacilli	0	200,000
5. Investigation of gonococcal susceptibility to penicillin	0	30,000
6. Investigation of systemic mycoses	0	100,000
7. Investigations on the ecology and control of arthropod-borne virus diseases	0	250,000
8. Measurement of dietary exposure to DDT and of its storage in human fat	0	18,000
9. Procurement of sera from specified patient categories, particularly those exotic or rare in the United States	0	15,000
10. Study of hospital microflora having minimal exposure to antibiotics	0	120,000
11. The study of leprosy in India	0	100,000
12. Collection and study of sera from animals in foreign countries to possibly identify naturally occurring treponematoses	0	20,000
13. Provision of sanitary shelter	0	100,000
14. Simple water supply equipment	0	75,000
15. Stabilization ponds and protein production	0	50,000
Total, India	0	1,228,000
Israel:		
1. Duration of immunity to rabies in vaccinated dogs	0	150,000
2. Investigation by fluorescent-tagged antibody techniques of the prevalence of gonococcal infection in the female and relation to complications	0	50,000
3. Investigation of gonococcal susceptibility to pencillin	0	30,000
4. Investigation of the problem of infections with atypical acid-fast bacilli	0	200,000
5. Investigations on listeriosis as a cause of abortion and neonatal disease in man	0	30,000
6. Measurement of dietary exposure to DDT and of its storage in human fat	0	18,000
7. Reuse of water	0	25,000
8. Evaporation control from surface of reservoirs	0	150,000
Total, Israel	0	653,000
Poland:		
1. *E. Coli* vaccine trials	0	120,000
2. Infant vaccination with attenuated polio-virus vaccine in Poland	0	54,000
3. Investigation of gonococcal susceptibility to penicillin	0	30,000
4. Investigations on the ecology and control of arthropod-borne virus diseases	0	250,000
5. Research on organic contaminants affecting water quality	0	250,000
Total, Poland	0	704,000

Bureau of State Services—Estimates using foreign currency—Continued

Country and projects	1961 estimate by project	1962 estimate by project
Yugoslavia:		
1. Anthrax investigations	0	75,000
2. Investigation of gonococcal susceptibility to penicillin	0	30,000
3. Investigation of the problem of infections with atypical acid-fast bacilli	0	200,000
4. Investigations on the ecology and control of arthropod-borne virus diseases	0	250,000
5. Rabies tissue culture vaccine investigations	0	20,000
6. Studies on the epidemiology and control of diarrheal diseases	0	350,000
7. Determinants of preventine health behavior of individuals	0	40,000
8. Basic studies of activated sludge treatment	0	150,000
Total, Yugoslavia	0	1,115,000
Total	0	3,700,000

National Library of Medicine.—Estimates using foreign currency

Country and projects	1961 estimate by project	1962 estimate by project
Israel:		
1. Translations and other services	0	$273,000
2. International Congress	0	2,000
Total, Israel	0	275,000
Poland:		
1. Translations and other services	0	174,500
2. International Congress	0	3,500
3. Reciprocal translations	0	35,000
Total, Poland	0	213,000
Yugoslavia:		
1. Translations and other services	0	152,500
2. International Congress	0	2,500
3. Reciprocal translations	0	20,000
Total, Yugoslavia	0	175,000
India: 1. International Congress	0	4,000
Total, India	0	4,000
Total	0	667,000

PARTICIPATION OF THE LIBRARY OF MEDICINE

Mr. Fogarty. The proposed participation by the Library of Medicine is new, also. Tell us about this program.

Mr. Murtaugh. Might I ask Mr. Adams, Deputy Director of the National Library of Medicine, who is here, to speak to this program?

Mr. Fogarty. Sure.

Mr. Adams. The $667,000 requested by the National Library of Medicine is intended primarily to continue translation projects mediated through the National Science Foundation, which has had access to these currencies under section 104(k) and has ongoing programs in Israel, Poland, and Yugoslavia. Incidentally, speaking with a little experience on the length of time it takes to establish arrangements, when I was with the National Science Foundation I had the job of establishing these contracts, and it takes anywhere from 9 months to a year to clear all of the necessary arrangements.

Mr. Fogarty. Some of us think it could be done in less time.

Mr. Adams. Well, I think, by and large, we have our own administrative difficulties squared away, but it is difficult working with the redtape requirements of the foreign governments.

Approximately $537,000 of the $667,000 requested would be transferred to the National Science Foundation to facilitate the continuation of these translation contracts. In addition, we would hope to commission the preparation of critical review papers, directories of foreign medical research institutions and personnel, and similar tools which would be of assistance in informing the American scientific public of the organization and facilities of medical research overseas in these countries.

Dr. Shannon. I might say, for the benefit of the committee and for the record, that this activity in translation and in preparation of critical monographs and of dictionaries and of listings of laboratories, and their research competencies, goes back to a program that was initiated about 3 or 4 years ago through the use of direct U.S. dollars. This program had as its initial objective the obtaining of current information on the activities of interest to us that were currently underway in Russia and were extended to some of the other languages with which our scientists are not generally conversant. This has been a very productive program and its extension represents an attempt on our part to make use of U.S.-owned foreign currencies that are already overseas, rather than hard U.S. dollars.

Mr. Marshall. If it were not for the efficiency of American agriculture, none of these funds would be available, is this not so?

Dr. Shannon. I am sure this is correct.

Mr. Marshall. As far as you are concerned, in carrying out the work of this program, if it were not for the availability of these funds, would you be doing any of this work?

Dr. Shannon. Yes, I think we would wish to undertake many of the projects that are proposed here, even if it required the use of hard U.S. dollars. On the other hand, we would feel that certain of these programs would be beyond our capabilities.

Mr. Marshall. As far as this program is concerned, it is purely a bookkeeping transaction, which enables us to utilize these foreign credits. Isn't that so?

Dr. Shannon. That is right. The point I would make, though, is that, as far as the country within which the funds are used is concerned, this represents an expansion of their currency. In our programs, however, we feel that the benefit is far overriding, as compared to the minor expansion and we hope that this would be the attitude of the countries involved.

Mr. Marshall. Have you ever made any estimate as to what proportion of the work that you are doing in these programs you would be doing if it were not for the availability of these funds?

Dr. Shannon. Well, Mr. Marshall, we don't know what we will be doing with these programs.

Mr. Marshall. Actually it would be a very small percentage?

Dr. Shannon. I suspect so, but it will only be possible to make that calculation after detailed project agreements are made and after the programs are underway. We would be glad to report back next year on that particular matter because this is of interest to us for straightforward operating considerations. I am sure it is of interest to the committee also, but we will have to have a year's experience with the operation before we can tell.

Mr. Fogarty. Had you finished the statement on your library program?

Mr. Adams. Yes. I would be very happy to answer further questions.

COSTS OF TRANSLATION

Mr. Fogarty. What about the costs of translation?

Mr. Adams. Under the existing contracts, these include the costs of both translation and publication of the material. They are approximately the same in dollars as the U.S. costs—a little less, possibly. U.S. costs run about $25 a page for the translation and publication of material; the Israel contract is about $22; the Polish contract is about $17. In Yugoslavia, the contract established by the National Science Foundation calls for translation only and not for the publication, so there is no real comparable figure.

Mr. Fogarty. So they are about comparable?

Mr. Adams. Comparable. Of course, the pricing of these in dollars is a function of the exchange rate at which these currencies are available.

Dr. Shannon. Mr. Fogarty, one might point out that there is one very definite advantage to this device of obtaining translations in this way, in that when one makes use of these foreign currencies for translation and printing in a foreign country, one has available to the contractor a type of scientific skill that is in very short supply in this country. In other words, it would be quite impossible to obtain certain of these translations, in the volume that would be required, in this country. There is thus an added benefit that goes far beyond the price. I would say that certain of the translations that will be undertaken just could not be done were we to attempt to do it locally.

THE INTERNATIONAL HEALTH RESEARCH ACT

Mr. Fogarty. Now you propose to add to the appropriation language the authority of the International Health Research Act. What is the significance of this?

Mr. Murtaugh. Would you wish to speak to that, Mr. Kelly?

Mr. Kelly. Well, when the language was drawn up, it was the intent to avail ourselves both of authorities under Public Law 480 and the authorities that were under the new International Research Act. It is going to be necessary, however, that we ask for a modification of the language as we submitted it to you, to put in the phrase "not otherwise provided for." We have drawn the language in such a way as to make it appear that this is the total utilization of funds for international research and that is not true. There are certain parts of the National Institutes of Health programs that utilize the authorities of the International Research Act, so we will have to put in "not otherwise provided for" in order to identify that.

FINANCING OF NIH INTERNATIONAL RESEARCH PROGRAM

Mr. Fogarty. We have in the record a statement on the international research programs of NIH, do we not?

Mr. KELLY. I believe so. It might be desirable at this point to indentify the appropriated funds we are spending for international purposes.

Mr. FOGARTY. Yes, please do that.

Dr. SHANNON. We submitted earlier a general summary of the international activity. Perhaps at this point we could summarize that in tabular form and refer it to the committee.

(The information requested follows:)

NIH international research and research training activities, fiscal year 1961

Activity	*Estimated obligations (in millions)*
Regular research and research training activities, total	$10.2
Research grants to foreign investigators	8.0
International fellowship program	.7
U.S. fellows studying abroad	1.5
Specialized activities under the International Health Research Act, total	5.0
International centers for medical research and training	2.4
Other international research and research training projects	2.6
Special foreign currency program, total	[1] 3.7

[1] Appropriated amount available until expended.

Mr. Denton?

AGREEMENTS GOVERNING USE OF FUNDS

Mr. DENTON. Do you have contracts or agreements to carry out these various research programs in the seven countries?

Mr. MURTAUGH. We are about to sign agreements on two projects in Israel, which will constitute the first two agreements we have been able to consummate successfully under the program this year.

Mr. DENTON. Do you have agreements with foreign countries to carry out research programs before you ask for the money or do you get the money and then try to get the programs?

Mr. MURTAUGH. Under the terms of the law under which this appropriation is presented, we must ask for a specific appropriation of these funds. It would be difficult to carry out discussions with the country without having some idea of the amount of moneys that would be available for this use.

Mr. DENTON. How do you know how much money you are going to need if you don't have some agreement with them?

Mr. MURTAUGH. The programs here have been developed on the basis of the interest of our scientists at NIH, the Bureau of State Services and other parts of the Public Health Service, in carrying out collaborative research activities on problems of mutual interest or where these countries present unusual opportunities for certain research studies.

Mr. DENTON. What I am trying to get at is this: I formerly served on the Foreign Operations Subcommittee of the Appropriations Committee and we got into a great deal of difficulty in foreign countries and we are in trouble in Laos right now because we gave them the money before they planned on what we were going to do with it. This caused a great deal of waste and extravagance. In appropriations to be spent in this country you can tell us what you are going to do with it, but when we have money spent in foreign countries, the agency requesting it doesn't seem to have any idea what they are going to do with the money they are asking for. I hope in your agency we won't get in that category.

Dr. Shannon. May I point out that these sums are calculated estimates of work that we know can be done in these countries because we know the scientists and laboratories that are available and we know their interest. The projects are an extension of work that is already underway in this country, so these are hard research proposals, but the mechanics, as such, present problems. We cannot undertake discussions with a foreign country for the use of funds that are partly in their custody without having an appropriation which is actually more of an authorization to proceed than a hard dollar grant to do so. In other words, these appropriations authorize us to negotiate within specified countries and within specified program outlines for the development of collaborative studies. There is nothing that is indicated here, or has gone into the calculation of these costs, that has not been thought through on our part. What is fuzzy is the detail of what will eventually come out of the negotiations. These negotiations are in the hands of our technicians at the National Institutes of Health, the Bureau of State Services, the National Library of Medicine, and the comparable technicians in the host countries in which these programs are proposed, so that this is not a loosely contrived hunting license.

Mr. Denton. When you want to set up a program, does it take the approval of the State Department?

Dr. Shannon. Not the detail of the foreign research activities involved. It does have the approval of the State Department in terms of their reviewing the general plan and saying whether it would be in the best interests of our country to support this type of research.

Mr. Denton. When do you get their consent?

Dr. Shannon. This is the first thing we obtain before we contact the foreign countries. This is done by negotiations with the State Department for a letter of intent from our Secretary of State to the American Ambassador of the country concerned saying the National Institutes of Health has proposed the following programs for discussion, and asking for embassy help in the negotiations.

Mr. Denton. I think it is very commendable to use the money you have over there. I think that is for a very good purpose. The only thing I hope that your agency doesn't do is to operate the way the International Cooperation Administration has operated for so long in requesting appropriations without adequate plans for its expenditure.

Dr. Shannon. Without drawing any comparison, I trust we turn over to this committee a very tightly administered program.

Mr. Denton. That is all.

Mr. Fogarty. Mr. Marshall?

BENEFITS OF THE PROGRAM

Mr. MARSHALL. I don't think that anyone can question the value to the United States from the standpoint of improving the health of the people throughout the world, but could you tell me what benefits have accrued to the American public as far as the American health is concerned from the expenditure of these funds?

Dr. SHANNON. Mr. Marshall, I would like to limit my remarks, if I may, to the program that we are proposing. These programs, in the aggregate, are not primarily designed as technical assistance programs for the host country, but, rather, as programs run out of our Institutes, out of our Bureau of State Services, out of our National Library of Medicine that we feel will facilitate the achievement of our national objectives. In these foreign countries, the population groups, the peculiar disease circumstances that are present, offer a rather unique opportunity for investigation. These programs should be clearly separated from the type of program that is undertaken solely for the benefit of the host country.

Now, it is true that there will be certain indirect benefits to the host country and I might point out a somewhat analogous situation: Insofar as we support research in medical schools, this is an indirect benefit to the educational process, but the primary justification for such expenditures is the development of a series of studies to achieve a very practical, discernible research objective. The incidental benefits are the benefits that accrue to the educational process. I think this is a precise parallel with these programs for the use of foreign currencies. They should not be looked upon as technical assistance or as assistance and development programs such as those that are the normal responsibility of the International Cooperation Administration.

Mr. MARSHALL. You are familiar with the purposes of representation allowances, are you not?

Dr. SHANNON. Yes, sir.

Mr. MARSHALL. Are any of these funds used in any way whatsoever related to representation allowances?

Dr. SHANNON. No, sir.

Mr. MARSHALL. No funds at all are used for that purpose?

Dr. SHANNON. None whatsoever.

Mr. FOGARTY. Mr. Michel?

TRANSLATION SERVICES

Mr. MICHEL. Mr. Adams, in this matter of translating, who, principally, does this translating? Are they medical scholars or is it done by professional translating agencies?

Mr. ADAMS. In each country concerned, there is an organization. In Israel this is performed with the assistance of the Israel Research Council; in Yugoslavia under the Yugoslavia Research Council; and in Poland under the State Central Institute for Scientific Documentation, I believe. It is a function of the Prime Minister's office in Poland. The requirements are that these semiofficial agencies in the country assemble the best scientific talent possible to do this translation, to check out its adequacy, to edit it very carefully, in accordance with our requirements.

Mr. MICHEL. In what principal languages are these publications which we want translated into English?

Mr. ADAMS. The contract in Israel calls for the translation of Russian scientific material and has already produced, in its approximately 18 months of existence, a considerable volume of translations which we have distributed to American medical libraries.

Mr. MICHEL. Would you folks put priority on the areas in which we know by intelligence sources or otherwise that we are behind, or would you spend the money to translate something which we knew about, say, 5 or 10 years ago and so would not perform any good useful function for the scientists in this country?

Mr. ADAMS. No, sir. We would make every effort to identify those specific works which had pertinence to American needs.

Dr. SHANNON. This is current literature.

Mr. ADAMS. Yes, these would be current works.

Mr. MICHEL. Do you want to go on?

Mr. ADAMS. In Yugoslavia the contract calls for the translation of Serbo-Croatian, but they have indicated a willingness to translate from other sources—Czech, Hungarian, and the like. In Poland the contract is exclusively for translation of Polish scientific materials. One interesting feature of the Polish contract is that we are engaged in a form of preventive translation, that is heading off the translation problem by encouraging the Poles to publish initially and simultaneously an English language edition of their principal scientific journals. This means, of course, that we will not have to translate after the fact.

Mr. MICHEL. Would you give us, for the record, a breakdown by countries of those funds for translating purposes?

Mr. ADAMS. I would be very happy to give that to you.

(The information requested follows:)

Distribution by country of funds for translating services

Country	Direct translations	Other translating services	Total
Israel	$262,000	$11,000	$273,000
Poland	136,000	73,500	209,500
Yugoslavia	139,000	33,500	172,500
Total	537,000	118,000	655,000

BEHAVIORAL STUDIES

Mr. MICHEL. On page 3 of your testimony you mention three areas, communicable disease and environmental health and behavioral studies. I think I know what you mean by the first two, but what are we referring to by the term "behavioral studies"?

Mr. MURTAUGH. I think that refers to a program to be conducted by the Bureau of States Services under Public Law 480. Dr. David Sencer from the Communicable Disease Center is here. Are you familiar with that?

Dr. SENCER. The specific proposal we have in mind would relate to Yugoslavia, where they have a different system of health services. One of our problems in this country is to find out why people accept health services or reject them. We would like to be able to do comparative studies in a relatively advanced country with a different method of providing services to see what cultural differences, what behavior differences block people from accepting services. This would be to the end that we could do a more efficient job of immunization, as an example, in this country.

Mr. Michel. But this would be a much more urgent requirement in underdeveloped countries than in one that is more advanced.

Dr. Sencer. Yes, sir; if we were thinking strictly of the technical assistance, it would be.

PROBLEMS IN NEGOTIATING AGREEMENTS

Mr. Michel. On page 7 you mention unresolved problems at the governmental level in one of the major countries—India. What would those unresolved problems be?

Mr. Murtaugh. Dr. Shannon spoke a moment ago to the nature of the problem that has arisen in India. We did have a team that carried out negotiations and discussions with the Ministry of Health and with the Medical Research Council in India during the latter part of November and December. Our prospects for development of collaborative projects looked very good. We had plans to send a negotiating team over during the early part of February to negotiate specific projects as agreed on under the prior arrangements that had been made, when we received a cable from the Ministry of Health in India stating that the question surrounding the use of these funds had been discussed between the Ministry of Health and the Ministry of Finance and that there appeared to be problems which were going to require cabinet level discussion and decision. This is the nature of the problem that still remains unresolved in India.

ADVANCE FINANCING OF PROJECTS

Mr. Michel. Page 200 in the justifications shows the differences between the estimate for 1961 and 1962. With the increased amounts that are in the overall increase, I note notwithstanding those increases that there is nothing at all for some diseases, like anemia and bladder cancer and so on, for 1962 whereas there was in 1961. Now what accounts for that?

Mr. Murtaugh. Now each of these amounts, sir, cover programs whose life may run from 3 to 5 years. In the case of pellagra and anemia projects, this is a program to be carried out through the National Institute of Arthritis and Metabolic Diseases in conjunction with the University of Cairo and the Navy Medical Research Unit No. 3 in Cairo. This will be a 3-year project and the total funds were made available to us in 1961.

Mr. Michel. In fiscal 1961?

Mr. Murtaugh. Yes.

Mr. Michel. That means that work is still continuing.

Mr. Murtaugh. That is right.

Mr. Michel. Now, would the same apply to those areas in India from item 13, say, through 22?

Mr. Murtaugh. Yes, it would.

Mr. Michel. Would all of these contracts run for a period of 3 years?

Mr. MURTAUGH. Three to five years, depending upon the nature of the investigation involved.

Dr. SHANNON. Mr. Michel, we must obtain a commitment from the host institution in the country for the spending of the money prior to the starting of the investigation so that the total program is funded during the initial year.

Mr. MICHEL. That is all, Mr. Chairman.

Mr. FOGARTY. Do you have anything else you would like to say?

Mr. MURTAUGH. No, sir. Thank you very much.

TUESDAY, APRIL 11, 1961.

NATIONAL HEALTH STATISTICS

WITNESSES

DR. FORREST E. LINDER, DIRECTOR, NATIONAL CENTER FOR HEALTH STATISTICS

DR. JAMES A. SHANNON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

HARRY L. DORAN, CHIEF FINANCE OFFICER

JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	1,323	1,716	2,059
Positions other than permanent	38	66	72
Other personnel compensation	33	32	4
Total personnel compensation	1,394	1,814	2,135
12 Personnel benefits	102	143	166
21 Travel and transportation of persons	82	165	206
22 Transportation of things	8	20	36
23 Rent, communications, and utilities	108	152	254
24 Printing and reproduction	70	85	98
25 Other services	263	284	378
Services of other agencies	939	1,191	1,251
26 Supplies and materials	26	37	57
31 Equipment	33	156	63
Subtotal	3,024	4,047	4,643
Deduct quarters and subsistence charges	1	1	1
Total obligations	3,023	4,046	4,642

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	243	297	342
Full-time equivalent of other positions	7	11	12
Average number of all employees	234	290	339
Number of employees at end of year	259	297	342
Average GS grade	6.6	6.6	6.9
Average GS salary	$5,715	$6,073	$6,238

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Operations (total program costs)	3, 036	4, 046	4, 642
2. Relation of costs to obligations: Costs financed from obligations of other years, net (−)	−13		
Total obligations	3, 023	4, 046	4, 642
Financing: Comparative transfers from (−) other accounts	−3, 023	−4, 046	
New obligational authority (appropriation)			4, 642

Mr. Fogarty. Next is "National health statistics." Dr. Linder, are you going to proceed on this?

Dr. Linder. Yes, sir. I also have with me the executive officer, who might be able to help me out.

Mr. Fogarty. All right, Doctor, go right ahead.

GENERAL STATEMENT

Dr. Linder. We have submitted a statement on the new item of national health statistics to the secretary and, if you wish, I could summarize that statement.

(Dr. Linder's full statement follows:)

Mr. Chairman and members of the committee, this is the first time the appropriation request before you under the heading "National health statistics" has appeared in this form. The major elements of the work carried out under this item are the activities of the National Health Survey, funds for which were previously included under "Salaries and expenses," and the activities of the National Office of Vital Statistics, funds for which were previously included in "Assistance to States, general."

The reasons for this new presentation deserve some explanation because it reflects, I believe, a more fundamental change than merely a budgetary or organizational reshuffling of existing activities.

FORMATION OF NATIONAL CENTER FOR HEALTH STATISTICS

The form of this appropriation request originates with the formation of the new National Center for Health Statistics which was established by the Surgeon General in August 1960. This Center consists of a new grouping of previously existing functions and certain other defined additional responsibilities, having as its major objectives a more unitary organization for the measurement of the health status of the Nation and for the research required for the identification of significant associations between characteristics of the population and health-related problems.

I think it may be said that there were two main reasons for establishing the Center.

The first of these is an operational reason. The National Health Survey and the National Office of Vital Statistics were previously independent units each concerned with parallel problems of data collection, data processing, statistical analysis, and fact dissemination. It was felt that putting both of these units under common technical direction could result in a more effective and productive coordinated organization. There could be a more useful internal exchange of operational resources and know-how with less compartmentalization of methods and facilities. For example, since its beginning in 1956, the work of the National Health Survey has been carried out very successfully on high-speed electronic computers, whereas the older procedures of the National Office of Vital Statistics have been tied to slower and less efficient accounting-type equipment. A single electronic computer facility, which is feasible under the Center's organization, will have substantial benefits for all elements of the Center's own program, and will provide the additional dividend of a useful resource for other units of the Public Health Service.

Also, still from the purely operational viewpoint, other units of the Public Health Service and the various State and local health agencies which cooperate with the Federal Government in the production of essential health data are involved in various data collection and data processing operations. A unitary and modernized statistical Center in the Public Health Service would constitute a focus of processing expertise, would stimulate throughout the Service the optimal use of technical and methodological innovations in the collection, processing, and anslysis of health statistics and would create a resource for technical assistance in these functions.

These operations reasons alone would fully justify the establishment of the National Center for Health Statistics, but the second reason for creating the Center is more compelling. This reason arises from the fact that there is a constantly and rapidly increasing need for better factual data as a basis for sound decision-making in the fields of medical and public health research and administration.

The need for an adequate factual base has long been recognized in the fields of agriculture, labor, foreign trade, production, and distribution and technically strong programs have existed in these fields in the Government for many years. But in the field of health we used to limp along with a hodge-podge of temporary ad hoc studies, rough estimates, and large areas of complete statistical ignorance.

Formerly one frequently heard questions raised regarding the general value of health statistics, as if the only justifiable purpose of such statistics was to establish some new dramatic medical discovery. Actually the uses of health statistics are more subtle and pervasive. In the complicated American system of public health and medicine, the users of health statistics include every element of the pattern—the public health legislator and administrator, the medical profession, the research worker, the National, State, and local official health offices, the voluntary health agencies, the life and medical insurance organizations, the manufacturers of medical supplies, industry and labor organizations, and many others. These organizations are coming to tighter grips with significant health problems—such as those related to costs of hospitalization, medical care of the aged, health insurance coverage of the population, distribution of the utilization of medical and dental services, the increasing impact of environmental factors on health. These questions, as matters for policy decision and action will remain with us indefinitely in one form or another.

It is for these reasons that there is an increased appreciation of the part that correctly collected and problem-oriented statistical analyses can play as the necessary foundation for sound planning and evaluation.

This, then, represents the second reason for the creation of the National Center for Health Statistics—to establish a Center which can give sustained and intensive attention to a comprehensive program for the production of the kind of health statistics facts now needed.

PROGRAM OF THE NATIONAL CENTER FOR HEALTH STATISTICS

The responsibilities of the Public Health Service in the field of health statistics were examined by the Surgeon General's Study Group on the Mission and Organization of the Public Health Service. Its final report states inter alia:

"The needs of the Nation and the responsibilities of the Public Health Service require broad regional and national data with respect to the character and dynamics of health problems, their trends and implications. While States and other organizations contribute valuable data, national intelligence requires a center for the collection, evaluation, analysis, and interpretation of data from many sources. The Public Health Service has primary responsibility at the Federal level to provide national intelligence on matters relating to health—births, deaths, illness, disability, health services, marriages, divorces.

"The shift of health problems from infectious diseases, population increases, population mobility, the fragmentation of health services, and the increasing complexity of the environment all present added difficulties in the development of intelligence adequate to meet current and future health needs. Thus, the Public Health Service has an urgent task in developing better ways to record and report basic health data, and to give them more rapid and meaningful interpretation."

The program of the Center, as defined in the final report of the study group is based on the following objectives:

1. To bring together the major components of the Public Health Service competence in the measurement of health status of the Nation and the identifica-

tion of significant associations between characteristics of the population and health-related problems.

2. Stimulate optimal use of technical and methodologic innovations in the collection, processing, and analysis of health statistics.

3. Create a resource for technical assistance in statistical data processing.

4. Associate closely the functions of collection, analysis, interpretation, and dissemination.

5. Permit expansion of health intelligence programs to correlate and interpret data from various sources.

6. Give better visibility to the national and international leadership of the Public Health Service in vital and health statistics.

These objectives are stated largely in functional terms. With regard to subject matter the responsibilities of the center cover the newer types of health data obtained from survey sources—morbidity data, incidence of accidents, disability, work-loss days, health insurance coverage, hospital discharges, medical costs, etc.—as well as those types of health statistics traditionally included in vital statistics—namely, birth, death, fetal-death, marriage and divorce statistics, and related studies.

From the point of view of methodology, the responsibilities of the center include the development and implementation of systems of health data processing and analysis; the continued improvement of survey methodology which is called for in the National Health Survey Act of 1956, and cooperation with the States in the solution of the technical and operating problems associated with vital records registration and analysis.

Following generally the recommendations of the Surgeon General's study group, this program of the center will be carried on by the Office of the Director of the center; two staff offices, the Office of Electronic Systems and the Office of Health Statistics Analysis; and two operating divisions, the National Office of Vital Statistics and the National Health Survey.

OFFICE OF ELECTRONIC SYSTEMS

A major continuing operational responsibility of the National Center for Health Statistics is the processing of extremely large volumes of health data on the prevalence and incidence of disease, data on births, deaths, neonatal deaths, marriage and divorce, and other factors relating to the health of the population. The Office of Electronic Systems is established with two major objectives: The first is to provide the organizational means for the modernization of the data processing activities of the center itself; the second is to serve as a focus for data processing expertise to encourage maximal use of technological innovations in data handling activities throughout the Public Health Service. The second of these objectives will be carried on in a nominal way during 1962 since our major effort in that year will be directed to the immediate and urgent problems of modernizing throughout the center its own data-processing work.

During the past 4 years the National Health Survey Division of the center has utilized the electronic computer facilities of the Bureau of the Census with highly successful results. In 1961 a plan for acquisition of computer facilities has been prepared and the gradual conversion of the tabulating work of the National Office of Vital Statistics to electronic computers is being started.

With the acquisition of computer facilities, and after a conversion period, the present tabulating work of the center can be carried on at essentially the present costs, but with the advantages that the work can gradually be brought to a current basis, the potential will exist for types of analytical work not possible heretofore, and some computer time will become available for use by other units of the Public Health Service.

OFFICE OF HEALTH STATISTICS ANALYSIS

The two operating divisions of the center produce a wide range of health statistics, but such statistics are tabulated primarily around individual topics. The function of the Office of Health Statistics Analysis is to analyze and interpret health statistics from various sources, carrying the analysis further than is done in the topical presentations of the National Office of Vital Statistics and the National Health Survey. This involves primarily the preparation of material analyzed with reference to major health program and policy problems rather than to singly defined topics. This extension of the analysis will greatly increase the utility and significance of the existing data to the research scientist, the public health administrator, and the legislator.

The Office of Health Statistics Analysis will also serve as the location for certain program planning activities of the center, such as the work of the existing National Committee for Vital and Health Statistics.

The present positions, funds, and functions of this Office represent a relocation of existing resources to the extent that such is possible at the present time. The estimates for 1962 include new funds relating to a special study on health trends of the aged. In 1962 an effort will be made to further develop the work of this Office by the identification and transfer to it of some of the existing analytical work now carried on in the operating divisions of the center, but which might be done more effectively under the broader terms of reference of this Office.

NATIONAL HEALTH SURVEY DIVISION

The health surveys were established by the National Health Survey Act of 1956 in recognition of the increasing and continuing need for up-to-date information on many aspects of the health of the American population. Since its establishment the National Health Survey has issued numerous reports on a wide range of topics, many of which have been mentioned previously to this committee. Current plans are extending the inquiries into such timely subjects as medical insurance coverage, cost of medical care, recuperation time subsequent to operations, health characteristics of the unemployed, and a variety of items based on health examinations such as medically established diagnoses and population distributions of physiological and physical variables.

There are three basic sources of data collection available to the National Health Survey. The first is by asking people about their health, the illnesses they have, the actions they have taken with regard to their health, and what the consequences of poor health have been. These types of data are collected in the continuing health interview survey which has proved to be productive of very valuable data on the demographic, social, and economic aspects of health.

The second source of data is based on actual physical and clinical examinations on a sample of the population. A survey of this design called the health examination survey, was initiated in fiscal 1960 and is continuing in 1961 and 1962. This survey is based on a smaller sample and for this reason does not give the demographic, social, and economic detail obtained from the interview survey, but does give a wide range of precise diagnostic material and population distributions of many physical and physiological variables never before obtained.

The third fundamental data source is the utilization on a sample basis of existing medical records, and thus is directed at the exploitation of the data now largely dormant in the files of hospitals and other institutions. The first two methods, requiring as they do contact with a population sample of individuals, are more elaborate and costly, but constitute the only methods for obtaining data on the health characteristics of the whole population. The third method, based on institutional records, is less costly and produces a different type of important statistics; namely, an operational type of data related to the utilization of medical care facilities and services. During 1961 preliminary designs for a health records survey are being drafted and the budget requests for 1962 include an increase for implementation of this survey.

The health records survey can be initiated more economically and expeditiously in 1962 than in any other year of the decade. The 1960 census will result in extensive and revised information on the institutions covered by the census. This information can form the basis for the sample selection of institutions and thus result in a more effective and up-to-date survey than if delayed until the census institutional information becomes obsolete.

NATIONAL OFFICE OF VITAL STATISTICS DIVISION

The functions of the National Office of Vital Statistics originated in 1904 when the Federal Government first began cooperation with the States in the improvement of vital registration and started what has now become the nationwide annual tabulations and analysis of vital statistics. I believe, Mr. Chairman, that this is one of the most long-standing and successful areas of Federal-State technical cooperation. By virtue of this period of Federal-State cooperation, the U.S. vital statistics system has achieved a high degree of technical development in certain respects, although it must be admitted that it retains serious deficiencies in other aspects.

In early decades of the system, vital statistics were merely routine and largely repetitive compilations of mass data. The introduction of sampling, the development of followback methods, and the custom designing of tabulations can permit studies of special topics as required, and can now introduce much more flexibility into the system.

More significant from a subject-matter viewpoint is the transition which is now taking place in the types of data being derived from vital statistics systems and the uses to which the available data are being put. For example, vital statistics were indispensable to the great progress made over the past decades in the control of infectious diseases. More recently, they have been widely used as basic indicators of problems and trends in the accident, cardiovascular disease, and cancer fields. Similarly, statistic of births and fetal deaths are being used to study intensively the causes of death and disability during the fetal and neonatal periods of life. Birth statistics and those of marriage and divorce are essential elements in the study of population growth and family formation.

The basic continuing responsibilities of the National Office of Vital Statistics for the regular collection, tabulation, analysis and publication of national annual vital statistics assume by far the greater part of available resources. The rapid growth of the population has added substantially to the volume of records (now approximately 6 million documents) which are processed, and it has become imperative to convert the methodology of data processing to modern procedures.

The 1962 estimates provide funds to bring the National Office of Vital Statistics data-processing methods into harmony with the electronic computer methods so successfully used by the national health survey. A necessary conversion of methodology, an overlap period with the older methods, and a complete reprograming of the vital statistics operations is involved.

The regular, comprehensive compilation of vital statistics for this country is the two-volume publication, "Vital Statistics of the United States," which is issued annually. It contains comprehensive and detailed vital statistics for the United States, individual States, and local areas. It is the basic statistical reference source for research workers and others concerned with the study of mortality, natality, fetal mortality, marriage, and divorce.

The period of the decennial census of population presents added requirements for the program of the National Office of Vital Statistics since definitive population figures for State and local areas are available only at this time. Accordingly, the 1962 estimates include funds for continuation of the work on census-related projects initiated in fiscal 1961 for the 1960 data years. These projects include (*a*) more detailed tabulations of 1960 vital statistics for geographic areas and with special attention to the mortality experience of the aged; (*b*) preparation of official U.S. decennial life tables; (*c*) statistical processing and analysis of a special sample of 1960 marriage and divorce transcripts; and (*d*) compilation of rates based on the 1960 census data.

The total appropriation estimate for 1962 is $4,642,000, or an increase of $595,700 over the amount available during the current year. I shall be glad to attempt to answer any questions that you may have relative to these programs.

Mr. FOGARTY. All right, go right ahead.

REASONS FOR ESTABLISHING NEW GROUPING

Dr. LINDER. Mr. Chairman and members of the committee, the appropriation request "National health statistics" reflects the formation in the Public Health Service of the new National Center for Health Statistics, which is a new grouping of previously existing functions and certain other defined additional responsibilities.

The formation of this center is a more fundamental forward step than merely an organizational reshuffling and arises from a new examination of the responsibilities of the Public Health Service in the field of health statistics which was made by the Surgeon General's Study Group on the Mission and Organization of the Public Health Service.

There are two main reasons for establishing the center. One is an operational reason—namely the various substantial data-handling activities engaged in by component parts of the center and many other units of the public health system—Federal and State and local level. As far as the center is concerned a common technical direction of its previously independent units will result in a more effective organization for data processing operations. Other units of the public health system could benefit also from the existence of a focus of data-processing expertise.

The second reason for establishing the center is the striking and constantly increasing need for better factual data by persons and agencies representing every element of the complicated American system of public health and medicine. These new needs arise from increased attention being given to such questions as duration and costs of hospitalization, medical care of the aged, health insurance coverage of the population and from a better acknowledgement of the fact that sound consideration of such problems rests on a basis of objective fact. It is the function of health statistics to provide this basis.

The work of the center will be carried out by the Office of the Director; two staff units, the Office of Electronic Systems and the Office of Health Statistics Analysis; and two operating divisions, the National Office of Vital Statistics and the National Health Survey.

OFFICE OF ELECTRONIC SYSTEMS

The Office of Electronic Systems is established with two major objectives—one, to provide for the modernization of the data processing activities of the center itself and, secondly, to serve as a focus to encourage the use of modern data-handling methods throughout the Public Health Service. Aside from the transitional period and its future advisory responsibilities, this Office will be financed largely from the existing level of funds.

The function of the Office of Health Statistics Analysis is the preparation of material analyzed with reference to major health programs and policy problems and data drawn from various sources, including those outside the center itself.

The National Health Survey conducts a variety of surveys for collecting up-to-date information on many aspects of the health of the American population. These include the health interview survey for collecting data on the demographic, social, and economic aspects of health; the health examination survey for collecting a wide range of precise diagnostic material and population distributions of physical and physiological variables; and the health records survey which is proposed for 1962 and which is based on existing medical records now lying largely dormant in the files of hospitals and other institutions.

The program of the National Office of Vital Statistics comprises the regular collection and analysis of the official nationwide data concerning births, deaths, marriages, and divorces; special studies relating to these events; and cooperation with the States in strengthening the State-Federal vital statistics system. The 1962 estimates for this Division provide new funds for the modernization and speeding up of its operating methods and for special help on projects relating to the 1960 decennial population census period.

The total appropriation estimate for 1962 is $4,642,000, or an increase of $595,700 over the amount available during the current year. This increase is to cover full year costs of the 1961 program of the National Health Survey, as well as the implementation of the health records survey and studies in the field of health status of the aged;

to provide funds for the National Office of Vital Statistics census-related work projects initiated in 1961, and for modernization of NOVS data processing methods.

Mr. Chairman, I will be glad to try to answer any questions you have on this program. I also brought with me a few charts which I think illustrate some of the significant kind of findings we get from these programs and if the committee is interested, I would be glad to show you some of these.

PROPOSED NATIONAL MEDICAL CLEARINGHOUSE

Mr. **FOGARTY**. Before I get to that, I would like to get back to Dr. Shannon before he leaves. It was brought to my attention—and I meant to bring it up a little earlier—that General Sarnoff, the RCA chairman, made a speech just recently suggesting that—

> through a blend of electronic computation and communication techniques, it would be possible to establish a National Medical Clearinghouse which could serve as a central repository for all the latest medical information. By a combination of communication circuits, every major hospital and medical school in the country could be tied into this clearinghouse.

Then he went on to say:

> That knowledge is being accumulated too rapidly for even the specialists to know a subject in its entirety. Research is done in a thousand places and one place has just reached the moment when something is found that can save a life. But that something has not worked its way into medical literature. Yet this one little fact might give a sick person a few more years of life.
>
> The top doctors, like the top men in any profession, are very busy and hard to get to. Hospitals do not readily interchange staffs. Nevertheless there is always one man, brilliant, imaginative, projecting his ideas far beyond the moment, who can save a life even by a suggestion. In the critical moments between life and death, the miraculous does occur, and the miraculous is often a great mind that hits the spot.

Then it gives some examples in connection with cancer and heart disease.

Have you people given any thought to establishing such a National Medical Clearinghouse, using all of these latest techniques—electronics and television and so on?

Dr. **SHANNON**. Mr. Fogarty, we have not envisioned the establishment of a center such as General Sarnoff proposes. This is something that could conceivably happen some time in the future. On the other hand, we have, together with certain of the other Federal agencies, undertaken very serious studies on problems of the storage and retrieval of information, which is the first step in a machine operation of this general sort.

Now, historically the broad responsibility for the storage and retrieval of information was given to the National Science Foundation, by Executive order, which designated this central agency within Government to approach these problems in a systematic fashion. On the other hand, we feel that we have such a very large stake in one of the broad areas of science that we have undertaken quite independently—not independently in the sense that there is lack of knowledge of what both groups are doing, but independently, in collaboration with the Library of Medicine—the systematic study of certain of the new tools that are available for this. The most recent action is a grant or contract under negotiation which would be supported by the National Heart Institute for the development of a machine for the storage and retrieval and sorting of information for the many special purposes that a mass of information can be used.

Let me give an example of what I mean. The primary publications today appear in a straightforward, competitive fashion in a whole array of abstract journals, yet no single abstract journal has the capability of filing and publishing all of the abstracts of all of the material available in the field. The contract being developed as a cooperative project with the National Library of Medicine envisages the development of a broad, basic compilation of information which then can undergo special sorting for those that might be interested in the advances in the development of blood pressure lowering agents or in recent development of new agents for psychopharmacology; another sorting might relate the new information that had accumulated in any given period of time concerning the origin of cancer. The development of machine techniques that permit the creation of a very broad memory and the ability to search in that memory in specific areas of science, is the first step that has to be taken prior to the development of a machine such as General Sarnoff says.

Mr. FOGARTY. He says, along those lines:

> If a doctor in a San Francisco hospital sought the source of information on a particular subject, he would simply dial a number. Instantly, a relevant bibliography would flash on a televisionlike screen before him. Then, when he made his choice of a particular article, he could dial again and get a microfilm version of the article on his screen.

Dr. SHANNON. Well, sir, all of this is possible. I think that this is in the realm of science of the future, if you will. I think that in fairness to what the National Library of Medicine is doing, one would not wish to compile all of the information that General Sarnoff says would be useful to compile; namely, compiling the bright ideas, on various subjects, of physicians all over the country in some central place for sorting out and then advising a specific physician in a specific situation.

Mr. FOGARTY. This was a story out of a newspaper. Now, I don't know whether he said you should accumulate all bright ideas. I don't think he actually meant that.

Dr. SHANNON. There has been too much emphasis on the ability to have access to ideas at too early a stage, prior to publication, prior to their systematic test by operation, prior to what I would call validation that the idea is in fact worthy of consideration.

Mr. FOGARTY. But I think you all agree that some of the knowledge we have now is not getting out into the field quickly enough.

Dr. SHANNON. This is correct, sir.

Mr. FOGARTY. This could overcome that, couldn't it?

Dr. SHANNON. Yes, sir; and this is the primary purpose of this contract we now are developing in cooperation with the National Library of Medicine. There is no doubt that information is now accumulating more rapidly than it can be digested by conventional means of coummunication. Library science techniques have not changed materially since the printing of the first book. There is the real danger, that solid new information will be lost and will not be available to people who need it unless there is a drastic modification of the way we store information and the way we make information available to our scientists. This is one of the more important activities being undertaken at the present time, and I would say, sir, the only criticism I have of the activity at the moment is that it probably should have started 4 or 5 years ago, rather than now.

Mr. Fogarty. Well, I guess you could say that about most of the things that you are doing at the Institutes of Health, couldn't you?

Dr. Shannon. Well, some of the things.

Mr. Fogarty. But I thought that he was just trying to make the point that we are not making use of all of the knowledge that we have available today and we should be thinking about these possibly much better methods.

Dr. Shannon. This is a very valid criticism.

Mr. Fogarty. Why don't you do something about it?

Dr. Shannon. We are.

Mr. Fogarty. I don't think it is a very good start if all you have is the one contract from the Heart Institute.

Dr. Shannon. We do have other grants, we do have other contracts, but this is a very——

Mr. Fogarty. Why not plan a new building and equip it to test out this theory.

Dr. Shannon. Well, sir; you couldn't design or equip the building with the present knowledge.

Mr. Fogarty. You couldn't?

Dr. Shannon. No, sir.

Mr. Fogarty. Could you start with a pilot project and use the Institutes of Health, as an example?

Dr. Shannon. Yes, a beginning could be made. I might point out, Mr. Fogarty, one of the problems here——

Mr. Fogarty. This is something new to you and I realize I took you unaware in asking about it. If you would like, I wish you would amplify on your statement and tell the committee just what could be done on a small scale and what facilities are needed and how much it would cost.

Dr. Shannon. This I would be glad to do, sir.

(The information requested follows:)

PILOT RESEARCH PROGRAM AT THE NATIONAL INSTITUTES OF HEALTH FOR ELECTRONIC DATA STORAGE AND RETRIEVAL OF MEDICAL RESEARCH INFORMATION

In recent years there have been dramatic developments in information processing and communication through the utilization of advanced systems concepts and electronic equipment. The goal described so ably by General Sarnoff may be considered as the ultimate achievement of what are now widely diversified research efforts. Undoubtedly these developments represent a very fruitful potential both in the conduct of medical research and in the transmission of results.

Efforts are now underway in many agencies, devoting large amounts of time, effort, and money in this field. However, these electronic devices accentuate some of the difficulties inherent in the designing of systems for information storage, retrieval, and dissemination. While the capabilities of electronic storage and retrieval methods and hardware are increasing at a formidable pace, the ability to utilize this potential is limited because of the complex conceptual problems involved. There exists, therefore, a great need for experimentation in this area. Among the challenging problems present are the development of systems, organizing and indexing of input and the means of distinguishing between significant and irrelevent information to be processed and communicated.

For several years the NIH has fostered and been engaged in the development and use of electronic data processing in a number of its scientific program and management activities. In addition, NIH has made a modest effort in advanced electronic communications. Primarily this has been in the field of closed-circuit television in conjunction with clinical procedures in the Clinical Center. As indicated by Dr. Shannon, the National Heart Institute is joining with the National Library of Medicine in the development of a machine system for storage and retrieval of medical information. NIH will continue to share a keen concern in this development.

There are a number of experiments which the NIH could profitably undertake to explore the use of electronic facilities for scientific data recording, processing, retrieving, displaying, and communicating. These projects would contribute to the larger problem and, in addition, provide benefits to the areas in which experiments are conducted. The projects could be conducted as an aspect of existing functions. The following indicate the general nature of typical projects within the capability of NIH which could be used to explore possible broader approaches in this field:

(1) Engage in a research program directed toward the utilization of advanced electronic techniques for the measurement, recording, communication, storage and retrieval of patient clinical information. This study would begin with the information acquisition, recording, storage and retrieval aspects of the Clinical Pathology functions of NIH's Clinical Center.

(2) Institute a system, as a development of machine technology, to provide rapid access in both scope and depth to information contained in published material resulting from NIH research programs both intramural and extramural. An existing manual system utilized for this purpose would be reoriented to the use of automatic data processing and presentation techniques and equipment.

(3) Construct an experimental pilot facility for the direct, real-time association of a constellation of laboratory equipment with a large-scale data processing system, possibly via an intermediate satellite automatic data processing system.

(4) Install a pilot system whereby one research group is equipped with a desk-size remote facility for immediate access to a sophisticated computation and data processing system.

(5) Establish a facility for the conversion of records and data, produced by biomedical instruments in the laboratory, to a form amenable to processing by automatic data processing equipment and other information storage and retrieval apparatus.

(6) Establish a facility for the conversion of quantitative records produced by automatic data processing instruments to a graphic form more amenable to interpretation by medical scientists.

During the first year these pilot projects would require an expenditure of approximately $1,250,000, including some nonrecurring costs. The second year needs would approximate $1 million. The undertaking of these pilot projects in the Bethesda area would require remodeling of existing space but for the present no new building is contemplated. It is likely that the extension of space proposed for Building 12 would be adequate for the initial stages of the above program.

DISSEMINATION OF MEDICAL INFORMATION

Mr. Fogarty. I was thinking back to a reception I went to yesterday for Dr. Papanicolaou. I remember meeting Dr. Papanicolaou back in 1954 in New York when he was awarded the Cancer Society Award. Dr. Scheele was then our Surgeon General. We asked about this smear technique that he had just developed and asked if it was worth spending some money on and he said it was. So we appropriated about $100,000 to start the project in Memphis, Tenn. As a result it is now being done all over the country. Was anything done prior to that by the Institutes of Health or by the Cancer Society to get this information out to the people?

Dr. Shannon. Well, the information was fairly well distributed through both scientific and medical journals and there was an awareness of the possibility. The problem here, on the other hand, was a very serious shortage of technicians who could examine slides, so that the technique was limited to a very small number of so-called cancer detection centers, like the clinic at the Memorial Hospital, and its counterparts in Chicago and San Francisco. I think that the main value of the funds that were expended in response to the interests of this committee were two: the first was the establishment of a series of clinics that used quite different social devices to get this diagnostic aid to the people. Memphis was the first, and there was one in Providence.

Mr. FOGARTY. We ran the one in Memphis 3 years and then turned it over to the local people.

Dr. SHANNON. Eventually there were 12 of the centers, not primarily to deliver the service, but rather to show how a service could be delivered, either via health department techniques, via social agencies, or via the county medical societies or the like.

Mr. FOGARTY. When we were able to get this money to start the project in my State, the Cancer Society and the medical profession got together; they developed a kit that was sent to every doctor in the State, giving an explanation of how this smear is taken and where it should be sent. As a result every doctor was brought up to date on the latest information we had because of this demonstration project in Memphis; and also through the leadership of the Cancer Society and the medical profession.

Dr. SHANNON. I think that this was true in many States. The second benefit was not only to learn how to do it, but the development of the informational pamphlets that went along with it, that encouraged the people to use the service which had been established within the normal medical practice; and the third benefit was the establishment of a training program that began to turn out enough technicians to satisfy the need that was generated. These were the three benefits of the program. The program was very successful to the point that some 2 or 3 years ago it was turned over to the Bureau of State Services by the National Institutes of Health for implementation in their normal State programs, which now carry it broadly across all of the States.

PUBLIC APATHY TOWARD PREVENTIVE MEDICINE

Mr. FOGARTY. After listening to some of the figures I listened to yesterday morning from the American Cancer Society, it seems to me that this discovery is going the way of the Salk vaccine. People just aren't going to their doctors for this examination or the doctors aren't talking enough about it to their own patients. They said the professional group of women, more than any other group, fail to take advantage of this.

Dr. SHANNON. It is one of the very serious matters that disturbs thoughtful people in the field of public health today, that the people, enlightened people in this country, are not making use of critically important diagnostic procedures or critically important preventive devices, where we have certain knowledge that a preventive device is effective; such as Salk vaccine which will prevent polio in the majority of cases, and the Papanicolaou smear test which will help to curtail cancer if done on a systematic basis—I won't say it will remove the disease as a hazard to life.

Mr. FOGARTY. I think they claimed yesterday it is about 99 percent curable if found early.

Dr. SHANNON. I don't know where the bottleneck is in this. I know that the Public Health Service has taken the polio situation as a case study to try to find out what retards the acceptance of this tool. I really don't think that all of the work that has gone into the polio vaccine as an individual vaccine is warranted if there aren't some lessons to be learned about the resistance to it. Vaccine is available in many cities through public clinics; it is there for the asking; it prevents a rather awesome disease in 90 percent or better of the patients and still you find that at the present time fully half or more of our preschool children are not vaccinated.

Mr. FOGARTY. It is over 50 percent, I think.

Dr. SHANNON. It doesn't make sense.

Mr. FOGARTY. It is just apathy on the part of the parents.

Dr. SHANNON. It is completely their responsibility because the public agencies, as such, the schools and the like can't get at these children who are the most susceptible age group.

Mr. FOGARTY. Dr. Porterfield, you were trying to say something.

Dr. PORTERFIELD. You brought up one limitation in General Sarnoff's farseeing and optimistic proposal and that is that he deals only with those clinicians who are interested and acute enough to ask for information and to know that there is a way or could be a way in which it could be gained. Now we have an even greater problem with material not just discovered yesterday and available through some new communications device, but information that has been available for sometime, like the Salk vaccine. The Public Health Service, as Dr. Shannon has said, is trying in other parts of the Service, to cope with this problem of motivation, both of professionals and of the general public, to use what is available in the way of resources.

BUDGET AMENDMENT

I would like to point out, if I may, in the amendment to our budget which has been sent up by the administration, there is, for example, almost $2 million to be spent in developing community methods of providing for people more fully the resources that are in those communities in the way of care, particularly, in this case, in the area of chronic diseases. It is through methods such as these, the educational devices, the technical assistance, the consultation by people from Federal to State to local communities that will do as much good in the long run as the general's system will do for the very alert clinicians in the medical centers. It isn't just the brandnew knowledge that needs exploitation.

Mr. FOGARTY. No, but the new could be combined with the old, couldn't it, in this system?

Dr. PORTERFIELD. This is in addition to the other things.

Mr. FOGARTY. Mr. Denton?

FOLLOWUP ON MEMPHIS CYTOLOGY PROJECT

Mr. DENTON. I have one question I wanted to ask which is kind of far afield, but you were talking about that Memphis program and the doctor down there that conducted it told me he thought they discontinued the test too soon, for this reason: He said that a great many women had cancer cells and didn't develop cancer, and some developed it later. But they found cancer cells where there was no cancer. He thought they had a history of a whole community, and if they followed it up, he thought it would be very valuable in finding about the spread of cancer, but they stopped it too soon.

Dr. SHANNON. I would be glad to find out the precise situation there, but that was not discontinued. It was discontinued as a demonstration clinic, but funds were left in the community for the followup of all cases that had been seen during the 6 or 7 years that the clinic was operating. What the results were, I do not know.

Mr. FOGARTY. Well, it was a 3-year program we planned when we appropriated the funds and then the Federal Government was to get out of it and let the local doctors take over, as they have in Memphis. Now it is up to the doctors.

Mr. DENTON. They had the Government there following statistics. They were still doing that and making records on that, but he thought there ought to be funds for the Government to follow up those cases and find out, where there were cancer cells but no cancer, if she developed cancer later.

Dr. SHANNON. Mr. Denton, you pose there a very serious problem that faces the Public Health Service every time it sets up a demonstration clinic or demonstration service of one sort or another. It is never set up unless it is felt that the forces existent in the community will carry through subsequently if the service proves to be highly effective. Now it was the judgment in Memphis that these forces for the continuation of that activity were there. Our continued study there related to a followup of what happened to individuals who had been examined during the test period, but, Mr. Denton, it would be most unwise for the Federal Government to attempt long term financing of all of the demonstration projects that are set up.

Mr. DENTON. I am just telling you what he told me, but I don't believe it will be followed up unless the Government does it.

Dr. SHANNON. The followup, I am sure, is going on and I will be glad to get a specific report on this for you.

ADDITIONAL POSITIONS BUDGETED FOR 1962

Mr. FOGARTY. Now, Doctor, there is $4,046,300 available for this activity in 1961 and the request for 1962 is $4,642,000, an increase of $595,700 and 45 positions. Will you provide for the record a complete breakdown of all of the positions and their grades and what they are?

Dr. LINDER. Yes.

(The information requested follows.)

Detail of new positions requested in fiscal year 1962

Grade	Position	Offices of the center[1]		National health survey		National office of vital statistics		Total	
		Number	Total salary	Number	Total salary	Number	Total salary	Number	Total salary
GS-14	Chief of branch			1	$12,230			1	$12,230
	Statistician					1	$12,230	1	12,230
GS-13	Survey statistician					3	31,950	3	31,950
	Analytical statistician			1	10,650	1	10,650	2	21,300
	EDP specialist					3	31,950	3	31,950
GS-12	Analytical statistician	1	$8,965	1	8,965			2	17,930
	Survey statistician			1	8,965	1	8,965	2	17,930
GS-11	Digital computer programer.			1	7,571			1	7,571
	Survey statistician					2	15,142	2	15,142
	Analytical statistician					3	22,713	3	22,713
	Health program specialist			1	7,571	3	22,713	4	30,284
GS-9	Statistician					2	12,896	2	12,896
	Health program specialist			2	12,896			2	12,896
GS-7	Administrative assistant			1	5,366			1	5,366
	Clerical assistant					2	10,732	2	10,732
	Digital computer programer.			2	10,732			2	10,732
	Health program specialist			1	5,366			1	5,366
GS-6	Administrative clerk			1	4,846			1	4,846
	Health survey assistant			2	9,692			2	9,692
GS-5	Clerical assistant	1	4,347	2	8,694			3	13,041
	Statistical clerk	1	4,347	1	4,347	1	4,347	3	13,041
GS-4	Fiscal clerk	1	4,056					1	4,056
	Secretary					1	4,056	1	4,056
	Total new positions	4	21,715	18	117,891	23	188,344	45	327,950

[1] Includes the Offices of the Director, Office of Health Statistics Analysis, and the Office of Electronic Systems.

INCREASE FOR THE OFFICE OF VITAL STATISTICS

Mr. Fogarty. Now you are requesting an increase of $289,200 for the Office of Vital Statistics. Is that for expansion of the present activity?

Dr. Linder. It involves some expansion of the program, particularly some special work that we have been asked to accelerate on studies of the aged and also some continuing work on projects that were related in 1960 to the census period, but a substantial portion of that increase is also for what I call the modernization of the activity, the data processing activity in the National Office of Vital Statistics.

Since the beginning, as you know, we have been using modern electronic computers for the National Health Survey work, but the National Office of Vital Statistics work is tied to older accounting type machines and I think it is imperative that we get both of these offices on the same basis and into more modern ways of doing our work.

Mr. Fogarty. Will you supply for the record what studies you want to do on the aging?

Dr. Linder. Yes, we can give you that.

(The matter referred to follows:)

Statement Regarding Projects in the Area of Health Care of the Aged To Be Conducted Within NCHS in Fiscal Year 1962

As a part of the general effort to improve the situation of the Department with regard to quantitative information relating to health care of the aged, the National Center for Health Statistics would carry out the following projects in the fiscal year 1962.

1. With the advice and assistance of the Division of Chronic Diseases and the Division of Hospital and Medical Facilities, initiate a study of patients in resident

medical institutions with particular reference to nursing homes. Mental hospitals, for which other data are available, would be excluded from this study. Although the content of the questionnaire has not been decided upon, it is likely that the information would include: length of stay, mobility, bed status, nursing requirements, diagnosis, and source of payment for the patients, and also certain characteristics of the institutions and their staffs.

2. Retabulate in greater detail for the older age groups some of the data collected within the past 3 years by the U.S. national health survey. The tabulations would include: length of stay in hospitals, proportion of hospital bill paid by insurance, bed disability at home, limitation of activity, medical and dental care, farm and nonfarm status, family living relationships, and family income.

3. Retabulate in greater detail for the older age groups some of the mortality data collected in the period, 1959–61, by the National Office of Vital Statistics. The tabulations would include: cause of death, county of residence, city of residence, State of birth for native-born and country of birth for the foreign-born, and age in single years instead of the usual 5-year age groupings.

4. Conduct within the newly created Office of Health Statistics Analysis special analyses and interpretations of trends in the medical care of the aged based upon health and vital statistics from the national health survey and the National Office of Vital Statistics and also from a wide variety of other sources.

NATIONAL HEALTH SURVEY

Mr. Fogarty. Almost all of the rest of the increase is for the national health survey.

Dr. Linder. That is right.

Mr. Fogarty. Why do you need $285,700 for that?

Dr. Linder. There, again, there are some special activities that we are accelerating in our regular program.

Mr. Fogarty. You better give us a breakdown of that.

Dr. Linder. Yes, I will do that.

(The matter referred to follows:)

National health survey

Detail of fiscal year 1962 program increases:	
Health examination survey	$93, 870
Health records survey	145, 000
Medical care of the aged	95, 000
Net savings in continuing program (primarily nonrecurring equipment purchases)	−48, 170
Total	285, 700

INFORMATION ON THE COST OF MEDICAL CARE

Mr. Fogarty. Now I notice you are planning to broaden the program to get information on the cost of medical care. Why can't you use the information available from the Bureau of Labor Statistics?

Dr. Linder. Their kind of information is somewhat different and doesn't go into the detail that we need.

Now another thing we will have to face is the question of going into more longitudinal studies of the cost of medical care. Our problem is not to get an index of medical care cost. This is the Bureau of Labor Statistics' function. But our problem is more to assay what the impact of medical care costs is on a family, not only through a cross section of time, but in a more longitudinal sense, over a longer period of time. Now we don't see how to approach this question yet, but this is one that the health insurance agencies are very anxious to have us approach and also people concerned with the medical benefits of organized groups of one kind or another, because it isn't enough to get a cross section of what a hospital bed costs or what a physician's visit costs; you have to get a distribution of how these costs group up on a particular family and don't group up on other families in order to get, as I say, an assay of what the maximum impact is of a medical illness event, so the approach is quite different from the BLS type activity and serves an entirely different need for statistical information.

Mr. Fogarty. Why don't you do it all then and get the Bureau of Labor Statistics out of this business?

Dr. Linder. I am not too familiar with what the BLS does, but I think what they do is merely one component of the general cost-of-living thing and if you are making a cost-of-living index covering all of the components of that, you have to put medical care in on the same comparable basis as you put the other components of cost of living, so I think they would have to continue the kind of work they are doing, but it is a distinctively different kind of thing than we hope to get into.

Mr. Fogarty. I am not too clear on the difference.

Dr. Linder. Well, let me try to make it clear in this way: From the kind of thing that BLS does, as I understand it, it is possible to get the average cost—that all of the people in this room, on the average, spend so much per year for medical costs—maybe $100, maybe $50. I don't know what the figure would be. But from the health point of view and from the impact on the family's point of view and from the insurance point of view and from the point of view of those groups that provide benefits to people, it is important to know whether everybody in this room has paid $50 or whether one person in this room has paid $500 and the other people paid nothing, because this determines the actuarial structure of what the impact of an illness is and it is this kind of information, it is the distribution of costs—what we call the frequency distribution of costs—which forms the acturial basis for any sort of medical insurance coverage or any sort of system that provides benefits to the individual and this also is the impact, is the measurement of the impact of illness on the family because, as you can see, the whole problem is different. If everybody in this room paid $50 a year, or if someone paid $1,000 and the rest of us pay nothing, and this comes up not of the average costs, not of the average cost-of-living costs, but of the differential frequency distribution from person to person or family to family.

Mr. Fogarty. Could that affect insurance and medical care programs?

Dr. Linder. Very definitely it could. As I said, this kind of information would form the actuarial basis for making any sort of medical insurance program a sound operation actuarially and financially and making it not just a rather hit-and-miss thing.

Mr. Fogarty. The Bureau of Labor Statistics doesn't do that for you?

Dr. Linder. No, sir, I don't think they do.

Mr. Fogarty. They could on a reimbursable basis?

Dr. Linder. There are many other little aspects of this cost of medical care that are sort of blanketed in. For instance, at the moment we are just completing a study in which we have taken a large number of cases of hospitalization and we have studied to see what proportion of the hospital bill has been paid by any form of insurance—has it been half of the hospital bill, has it been all of it, has it been none of it? This is something entirely out of the BLS terms of reference and their method of operation.

Also, to carry the point a little further, the health records survey we hope to develop starting next year is an attempt to go into the records now existing in medical institutions and from the analysis of those records determine a number of things, one of which might be the distribution of costs relating to that hospitalization or institutionalization. This requires working with medical institutions and again is not in the pattern of the BLS cost-of-living-type surveys.

Mr. Fogarty. Mr. Marshall?

POSSIBLE SAVINGS AS A RESULT OF CONSOLIDATION

Mr. Marshall. On the first page of your summary statement you state—

> the appropriation request for national health statistics reflects the formation in the Public Health Service of the new National Center for Health Statistics, which is a new grouping of previously existing functions and certain other defined additional responsibilities.

Were you able to avoid some duplication by this new grouping?

Dr. Linder. Well, I think we will. It can't be done overnight because the essential avoidance of duplication comes out of the fact that we are establishing this Office of Electronic Systems, which is a high-speed, modern computer installation, and both units will use this system.

Now the problem there is that the transition period of getting from the old procedures to the new procedures is something that will take us almost 3 years but this will ultimately make us more effective and avoid a duplication of facilities in the two divisions.

Mr. Marshall. On page 2 of your statement you talk about the electronic systems. Will you be able to so coordinate your work that you will need less electronic equipment than you did formerly?

Dr. Linder. Well, at the present time we don't have any electronic equipment. In the National Health Survey, we are using the facilities of the Bureau of the Census on a part-time basis and in the National Office of Vital Statistics we are using accounting-type equipment. When we put it together, after the transitional period, where there is necessarily some overlap, you see, of method, when we put it together the cost of the new system will be essentially the same as the cost of the old system, except we will have many by products—advantageous byproducts of the new system that we can't have under the present system.

For example, we have many customers within the Public Health Service that will want to use our system and our equipment and there will be a servicewide advantage.

Mr. Marshall. In light of the fact that there may be some possibilities of saving some personnel and money in connection with the gathering of statistics, shouldn't this committee look toward a reduction, rather than an increase in the amount of your appropriation?

EXPANSION OF ACTIVITIES

Dr. Linder. On a strictly comparable program, that would be the case, but the National Center of Health Statistics, I think, was created with the idea that its responsibilities and its activities should go beyond just merely putting together administratively two existing things.

Mr. MARSHALL. Would you place in the record at this point some of the things that you expect to do as an enlargement of the activity?

Dr. LINDER. Yes, sir.

(The information requested follows:)

STATEMENT ON BROAD AREAS OF FUTURE REQUIREMENTS FOR HEALTH STATISTICS

The National Center for Health Statistics (NCHS) was established in fiscal 1961 after a reconsideration by the Surgeon General of the responsibilities of the Public Health Service in this field. This center was established partly to effect more efficient management of existing work but perhaps more in response to rapidly increasing requirements for more adequate data relevant to changing health problems. These needs were stated by the Surgeon General's Study Group on Mission and Organization of the Public Health Service as follows:

"The needs of the Nation and the responsibilities of the Public Health Service require broad regional and national data with respect to the character and dynamics of health problems, their trends and implications. While States and other organizations contribute valuable data, national intelligence requires a center for the collection, evaluation, analysis, and interpretation of data from many sources. The Public Health Service has primary responsibility at the Federal level to provide national intelligence on matters relating to health—births, deaths, illness, disability, health services, marriages, divorces.

"The shift of health problems from infectious diseases, population increases, population mobility, the fragmentation of health services, and the increasing complexity of the environment all present added difficulties in the development of intelligence adequate to meet current and future health needs. Thus, the Public Health Service has an urgent task in developing better ways to record and report basic health data; and to give them more rapid and meaningful interpretation.

"Although the basic recording of vital data is a State function, the national and international significance of such data is so great that the Public Health Service should use every appropriate means to improve the accuracy and completeness of information reported. It should actively explore alternatives or supplementary ways for the more rapid transmission of information from States and localities. The National Health Survey represents an important step in development of more comprehensive data relating to the health status of the American people.

"A number of functions of the Service could be carried on more effectively through the utilization of modern high-speed computer techniques. There are some functions whose development will depend upon the utilization of such techniques. The work of the National Office of Vital Statistics could be markedly accelerated by such means, which would make possible analyses of considerable value to the Service and the Nation.

"The Public Health Service should develop strong leadership in the use of systems of data processing and analysis. To this end it should train the necessary personnel, acquire or have access to the necessary equipment, and develop methods to make maximum use of the potential of such equipment.

"While there are immediate national needs that can best be met on an intramural basis, the Service should also work with and support other groups in adapting newer statistical techniques to the solution of health problems.

"The National Center for Health Statistics will bring together the major components of Public Health Service competence in the measurement of health status of the Nation and the identification of significant associations between characteristics of the population and health-related problems. Further objectives are to—

"Stimulate optimal use of technical and methodologic innovations in the collection, processing, and analysis of health statistics;

"Create a resource for technical assistance in statistical data processing;

"Associate closely the functions of collection, analysis, interpretation, and dissemination

"Permit expansion of health intelligence programs to correlate and interpret data from various sources; and

"Give better visibility to the national and international leadership of the Public Health Service in vital and health statistics."

The translation of these general objectives to useful results requires an examination and reorientation of every facet of the Center's program and the expansion of activities carried on only in a nominal way at the present. The required areas of new work are indicated in broad outline in the paragraphs below.

Health statistics analysis.—The Center produces a large variety of data relating to births, deaths, marriage and divorce, illness, accidents, hospitalization, disability and other factors relating to health and medical care. These data are presented in detail with the accuracy and precision possible under present scientific methods of data collection—mostly in topical reports with the information classified by many demographic, social, and economic variables. While it is not the function of the statistician to point out the implications of these data for policy decisions, it is a proper responsibility to analyze the body of data to an extent sufficient to make its factual meaning evident. For example, there has been great interest recently in the trend of the crude death rate in the United States with some concern that it has not shown any reduction in recent years. A further analysis of the death rate, taking proper account of the changing composition of the population would show a continuing decline in most age groups—presumably in response to increased public health activities.

Such analysis of data, properly comparing our data with those in other countries, developing more sophisticated indexes of health trends, and relating our data more systematically to major problem and policy questions is an important aspect of the Center's future program.

Vital statistics.—The U.S. vital statistics system is a joint Federal-State activity with the States having responsibility for financing and administering the collection of basic data and the U.S. Government the responsibility for national compilation and promoting intrastate development and comparability. Since States are facing the same increasing requirements and new technical problems as the U.S. Public Health Service, there is an obligation to increase the advisory, coordinating, and developmental services that the NCHS provides the States.

This need ties in with the present evolution in the vital statistics field, expanding the scope of the work from the routine compilation of traditional types of data to newer flexible studies that can be more responsive to current needs. These newer approaches, which will be carried out as a part of the Center's future program involve special surveys based on vital records. These surveys will have the effect of greatly increasing the information available, without overburdening the legal aspects of the vital records system with statistical items. Similar efficient exploitation of the present records by matching records will permit new analyses of interrelated variables. For example, the new problems related to radiation raise questions regarding the possible genetic effect of medical X-rays exposure. A followback on a sample of birth certificates can reconstruct the X-ray history of the mother and this can be related to defects reported on the birth certificates. Then matching of the birth records with infant death certificates can trace any possible relation to infant mortality rates.

The technical problems of these types of studies have been solved and their effective contribution has been demonstrated. The expansion of vital record-linked sample studies is an essential part of the future program of the NCHS to revitalize the NOVS.

The regular collection of birth and death data has, of course, been long established, but this is not the case with marriage and divorce statistics, which are just now emerging from their most elementary stages. In the past several years the basic registration areas have been established and a pilot compilation of data based on a small sample has been carried on. The sample size of this work should be substantially increased to achieve a greater precision in the data—and this required improvement of the marriage statistics of the United States should be completed in time for the greatly increased attention that will be given to these data when the coming boom in marriages materializes.

Health surveys.—The various surveys conducted by the National Health Survey Division under the Health Survey Act of 1956 constitute a major and growing aspect of the program of the National Center for Health Statistics. These surveys have proved most effective in developing needed new areas of health data particularly through the continuing interview and examination surveys. Here, however, the future program contemplates certain additional types of surveys as well as modification and extension of the present activities.

Major future requirements are the development of sample data-collection devices utilizing existing records in hospitals and medical-type resident institutions. From such sources data bearing on the characteristics of persons institutionalized, on causes, duration, and treatment, and other information on institutional services and their costs can be obtained. These surveys are in the design stages and will constitute a valuable future addition to the survey program.

Other surveys now established on a continuing basis will require redesign to take account of changes in population composition and distribution and extension into new subject matter areas. One particular example of this is the health examination survey which is now limited to adults of ages 18–79. Modification of this survey to cover children is planned for the near future.

Affecting every aspect of the survey programs, as the range of collected data expands, is the need for an accelerated program of studies in survey method as specifically provided for in the act. The initial and limited surveys started in 1957 drew from a fund of methodological know-how which had been built up over a number of previous years. The rapid expansion of demands for new types of data from the surveys has not been paralleled by an expansion of technical research. It is considered essential that this research be expanded to avoid the risk that the surveys will, in the future, fail to provide the scope and quality of information expected from this program.

Data processing.—The data-processing problems of the Center itself and the conversion of its own procedures to modern methods can, after a transition period, be handled as a part of the program expansions indicated above. The responsibilities of the National Center for Health Statistics to become "* * * a resource for technical assistance in statistical data processing" implies a future expansion in order to provide expert consultation and computer services to other units of the public health system.

MORTALITY RATE AT NIH CLINICAL CENTER

Mr. MARSHALL. Now, I intended to ask Dr. Shannon this, but it probably comes in your department. Could you supply for the record the mortality rate of patients in the National Institutes of Health Clinical Center?

Dr. LINDER. Well, I would have to get this from Dr. Shannon.

I think the type of statistics may be a little deceptive whichever way the figures show because—I am not in the Institute, so I can't speak for them—but the population of the National Institutes of Health clinical centers is not a cross section population of people in the United States that are hospitalized and any conclusion that you would make from comparing the mortality case rate there with any other institution would, from a statistician's point of view, be misleading rather than informative.

Mr. MARSHALL. That is all.

Dr. PORTERFIELD. We can supply this material if we may add some discussions to the actual figures in order to bring out the reasons why they may be unique, if they are.

NOTE.—The mortality rate for clinical center patients, based on gross discharges, was 7.43 percent for fiscal year 1960.

Mr. FOGARTY. Mr. Michel?

OPTIMUM SIZE AND COMPOSITION OF A SURVEY OR SAMPLE

Mr. MICHEL. Doctor, what do you consider to be a good sample for your statistics, percentagewise?

Dr. LINDER. I guess this is a question no sampling expert will permit himself to answer because it varies entirely with the problem that you are dealing with. Now, the first requirement for a good sample is, the first thing is that it is representative of the population group that you are talking about. I think this is the unique contribution of the National Health Survey activity, that we are always talking about the American people; we are not talking about a group of volunteers or a group of hospital people and/or any selected group like that.

The size of the sample depends upon two things: (1) On how much precision is required in terms of the action that people might take on the basis of the facts. In some cases you need very great precision and in other cases an approximation is good enough. The action you would take, the decisions you would make wouldn't make any difference.

Mr. MICHEL. Give me an example of the two extremes. If we are looking for precision now, what has your department said is a minimum standard for a sampling?

Dr. LINDER. Yes. Now, I will give you some examples. In the health interview survey, which is our continuing survey, we go out to every State in the country and ask people questions about their health, what they did about it, what effect it had on them. Here we have a sample of about 120,000 people a year. Now, this is not too big. This will give us a national estimate, but we can't get State estimates.

Mr. MICHEL. Does this item of $41,200 for travel, for health examination survey teams have anything to do with what you were just talking about?

Dr. LINDER. That can have to do with the next example. In the health examination, sir, where we take a mobile clinical facility, moving it around the country from stand to stand, there our sample is as small as 6,000 examinations over the country as a whole and this is because here we are making rather precise clinical diagnostic-type measurements and blood pressure measurements and things like that, where the error is fairly small and we don't intend to cross-tabulate the material by a greater variety of different variables. Six thousand is about the minimum that we could use for that kind of study and we need 120,000 as a minimum as the other study because there we cross-tabulate that information by age, by sex, by income, by education, by urban-rural residence, by farm and nonfarm, and a great variety of other cross-tabulations, so that the sample breaks down very quickly—fragments quickly into little pieces.

Mr. MICHEL. As the population increases, your figure of sampling has to increase, too, does it not?

Dr. LINDER. No, sir. To the sampling theory, the only thing that counts is the size of the sample and the size of the population you are drawing it from doesn't make any difference.

Mr. MICHEL. You don't deal in percentages at all?

Dr. LINDER. No, sir.

Mr. MICHEL. And that is a rule of thumb for the statistician?

Dr. LINDER. Yes, sir. The percentage is just a popular way of speaking. Lots of people use that. But the thing that counts is the total aggregate in the sample and the variation that is in that sample.

Now, the variation is really the important thing. If everybody in the United States were exactly the same, you would take one person and measure him and look at him and you would know everything because everybody is the same and that sample of one would be completely scientifically correct and precise. When people start varying, then you need the increase in the size of the sample. The statistical technique is to study the amount of the variation and from that determine the size of sample that is required to get the precision that you think the situation demands.

Mr. Michel. Then in future years there would be no reason for you to ask for increased funds to carry on this work, because of an increase in population?

Dr. Linder. Not because of an increase in population. If we want more precision, if we want to tabulate our material by State or other finer groups, then I will come back and argue we need a bigger sample.

Mr. Michel. Do you think that is necessary now?

Dr. Linder. I would rather keep the sample at the size it is for some time. There are lots of people that want us to do things our sample won't let us do, but I think that the program needs a longer shakedown cruise and I would not argue that, with the exception of one small area of our work and that is the marriage and divorce statistics.

Mr. Michel. Why would you single that out?

Dr. Linder. The marriage and divorce statistics is now operating on a sample of 45,000 records from all over the country.

Mr. Michel. 45,000?

Dr. Linder. 45,000, and this is pitifully small and we have been criticized strongly by the people interested in this kind of information that this is not enough because you have to cross-tabulate this by age and length of marriage and a number of other characteristics and our sample here is definitely too small.

STUDIES OF HOSPITAL INSURANCE

Mr. Michel. You mentioned earlier a study in the area of health insurance and what portion of hospitalization was covered by health insurance. Did you initiate this study on your own or were you pushed into this by the medical profession or by a hospital association or any other outside group?

Dr. Linder. I don't think it was really on the instigation of a pressure group, but in the national health survey we have an advisory committee made up of users of statistics—not technicians, not statisticians, but customers of our material—and this advisory group consists of about 25 people. They come from the life insurance field, the health insurance field, the drug manufacturing field, the market research field, the medical profession, the dental profession, the nursing profession, the public health profession, and the whole range of people that are concerned with any aspect of health problems in the American public. This group meets once a year and we tell them what we have done; we solicit their advice on where we should go, what areas have the greatest priority in our work and I must say that for several years there has not been disagreement in this group that we ought to go further and faster into the areas that might be called medical economics, like the insurance field, the cost of medical care and these kinds of things.

Mr. Michel. Will that study go so far as to indicate whether or not an individual's hospital bill varies depending upon whether he has hospital insurance and the degree to which he has it? I get a criticism that you go into the hospital and the first thing you are asked is whether or not you have insurance. There is enough suspicion among some to believe that because one has it the bill is increased and that if one had none at all the bill would be lower.

Dr. Linder. I don't think we should properly venture into this field.

Mr. MICHEL. Why not?

Dr. LINDER. I think that the correct answer to that question would involve—and perhaps Dr. Porterfield can contribute to this point—would involve more of a medical audit of really what was done in the hospital, a detailed medical audit of what was going on there.

Mr. MICHEL. In your statistical division then, you have no plan for getting into this field?

Dr. LINDER. I think it would be inappropriate for us to get into this field. This, it would seem to me, would be more in the realm of the American Hospital Association, American Medical Association, and I don't think that a statistician should get into the business of a medical audit. Maybe it is appropriate for somebody else in the Public Health Service, but it is a medical problem and not a statistical problem.

FACTORS AFFECTING MEDICAL COSTS

Mr. MICHEL. Have you made any studies that would indicate medical costs per family broken down by various income categories?

Dr. LINDER. Yes, income is one of our standard economic items, and when we get into the cost field—we are not doing that now very much; we are just venturing into it because it is extremely complicated and difficult and technically there is lots we don't know about how to do it, but in the things we are now doing, like the number of dental visits that people have per year, the number of physician visits they have per year, the fact of whether or not they had medical insurance, these items we have by income groups and we publish this information.

Mr. MICHEL. Would they go so far as to indicate whether or not there is a direct correlation between income and the number of children that get vaccinated or inoculated for various diseases?

Dr. LINDER. We haven't checked anything on inoculation programs yet, but if we put that into our questionnaire why we can certainly look at that in the income groups; yes, sir.

Mr. MICHEL. It would seem to me that would be a very appropriate area.

Dr. PORTERFIELD. Mr. Michel, the Public Health Service is approaching several of the questions you have raised, not in the National Center for Health Statistics and not by the same kind of precise sampling and statistical enumeration that Dr. Linder is responsible for, but by studies of practices that are going on and I can describe a few of those, either now or when we come to the next item in the hearing.

METHODS USED TO AVOID DUPLICATION OF STATISTICAL WORK

Mr. MICHEL. I think in answer to the chairman's question you replied that you weren't completely familiar with what BLS was actually doing in the area of determining trends in costs of medical care. If you don't know, then how would you be able to render a determination whether or not you were duplicating one another's work?

Dr. LINDER. There is in the Bureau of the Budget an Office of Statistical Standards. This is not an estimation operation, but an office that has the responsibility of insuring that the Government agencies are not duplicating each other and are not in competition with each other. They have very strong coordinating powers and the Office of Statistical Standards there is very closely informed as to what we are doing, what we intend to do and also very closely informed what BLS is doing, so we do have a mechanism that assures the fact that there is not any duplication of effort or intent on these various things.

Mr. Michel. And you advise them periodically what areas you are going into?

Dr. Linder. Yes. I meet with them. They have a person who is regularly assigned to our work, day-to-day contact. We talk on the telephone or he comes over, but more formally than that, I meet at least once a year with the advisory committees of this office and explain our program to them.

I just met a couple of weeks ago with the Labor Advisory Committee on Statistics of the Office of Statistical Standards of the Bureau of the Budget and described our whole program to them, so our communication and our relationships with the Office of Statistical Standards and with these other agencies is very close. We actually do some things on request from the Labor Department.

For example, we are adding to our questionnaire next July an item on unemployment because there has been a specific request that we try to characterize the health features of the unemployed group, what are the health characteristics of this unemployed group. At the request of these people we are adding this item this year.

Mr. Michel. That is all, Mr. Chairman.

Mr. Fogarty. Do you have anything else you would like to say, Doctor?

Dr. Linder. No, sir.

Mr. Fogarty. Thank you very much.

FRIDAY, MARCH 24, 1961.

OPERATIONS, NATIONAL LIBRARY OF MEDICINE

WITNESSES

DR. FRANK B. ROGERS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE
DR. LUTHER L. TERRY, SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	1,103	1,229	1,268
Positions other than permanent	6	8	8
Other personnel compensation	40	17	12
Total personnel compensation	1,149	1,254	1,288
12 Personnel benefits	75	93	96
21 Travel and transportation of persons	10	12	17
22 Transportation of things	2	2	5
23 Rent, communications, and utilities	41	43	90
24 Printing and reproduction	92	144	98
25 Other services	29	35	38
Payment to "National Institutes of Health management fund"	--------	--------	265
26 Supplies and materials	48	64	71
31 Equipment	90	92	98
Total obligations	1,537	1,738	2,069

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	224	224	233
Full-time equivalent of other positions	1	1	1
Average number of all employees	214	214	222
Number of employees at end of year	215	214	226
Average GS grade	6.3	6.3	6.2
Average GS salary	$5,256	$5,714	$5,664
Average salary of ungraded positions	$4,134	$4,039	$4,039

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Operations (total program costs)	1,551	1,743	2,066
2. Relation of costs to obligations: Costs financed from obligations of other years, net (−)	−14	−5	--------
Total obligations	1,537	1,738	2,066
Financing: Unobligated balance lapsing	29	--------	--------
New obligational authority	1,566	1,738	2,066
New obligational authority:			
Appropriation	1,566	1,662	2,066
Proposed supplemental due to pay increase	--------	76	--------

General Statement

Mr. Fogarty. We have with us next the National Library of Medicine. Dr. Rogers, do you have a statement for the committee?

Dr. Rogers. I have a prepared statement I will leave here.

(Dr. Rogers' prepared statement follows:)

Operations, National Library of Medicine

Mr. Chairman and members of the committee, at the end of fiscal year 1960 the steadily expanding collections of the National Library of Medicine numbered 1,049,261 pieces, representing an irreplaceable collection of medical literature of all times, from all places, and in all languages. Greater use was made of these materials in medical and related fields by physicians, dentists, public health workers, educators, and workers in every field of health than at any time in the past decade.

INTERLIBRARY LOAN SERVICES

Through interlibrary loan to other libraries the National Library of Medicine makes its material available worldwide to all who have need for this service. The 95,595 interlibrary loans furnished in 1960 to physicians and other health workers through approximately 1,700 libraries represent an increase of 31 percent over the previous year. So far this year requests for loan of materials have been 18 percent greater than the comparable period last year. The program for converting to microfilm parts of the collection which are disintegrating as the result of heavy use or the poor quality of the paper used in its printing was curtailed by approximately half a million pages due to the sharp increase in interlibrary loan requests.

INDEXING SERVICES

It was reported last year that the January 1960 issue of the Index Medicus was the first issue of the Library's monthly index of medical literature to be prepared under the new mechanized copy preparation system. During the first year of operation, coverage of the Index Medicus increased to 125,000 journal articles indexed from 1,677 journals, an increase of 17 percent over articles indexed the previous calendar year. Coverage is expected to rise in 1961 to 135,000, and in 1962 to 150,000 journal articles. Work has been completed at the Library on the first annual Cumulated Index Medicus which will be published this spring.

PUBLICATIONS PROCUREMENT AND INTERNATIONAL EXCHANGE

The year's literature acquisition activities resulted in substantial increases in the Library's accessions. New exchange arrangements were established with 11 institutions handling publications from the U.S.S.R., publications were received from 23 Soviet institutions without exchange agreement, and 52 new Russian serial titles were added to the collection. The Library now maintains exchange relations with more than 1,000 institutions outside the United States.

PUBLICATIONS PROGRAM

Major bibliographic aids prepared by the Library during the past year include: Bibliography of Medical Reviews, listing 3,241 review articles; National Library of Medicine Catalog, 1955–59, listing 238,752 author and subject entries, including the year's increment of 18,168 new main entries; Film Reference Guide to Medicine and Allied Sciences, listing 1,991 current film titles; and the Index Medicus.

In addition to these major bibliographical aids, 151 special bibliographies were prepared in 1960, on subjects such as "Arthropod-Borne Encephalitis"; "Biological Effects of Non-Ionizing Radiation"; "Leptospirosis"; "Narcotic Addiction"; and "Viral Genetics."

Bibliographies published or planned for publication in 1961 include: "Russian Drug Index"; "Salmonella Infections"; "National Medical Bibliographies"; "Medical Dictionaries"; "Russian Surgical Suturing Apparatus"; "Toxoplasmosis"; "Medical Newspapers"; "Normal Pathophysiology of Aging"; and volumes II and III of the final series of the "Index Catalogue."

PROGRAM STATISTICS

During fiscal year 1960 the Library acquired 16,028 books and added 1,090 new serial titles; it purchased 420 old and rare items for its history of medicine collections, cataloged 22,395 titles, and added 2,302 pictures and portraits to its medical art collection. There were 135,366 volumes circulated to users of the Library; 9,046 reference questions were answered. Over 2 million pages of medical literature were microfilmed in response to requests, and an additional 1.2 million pages were microfilmed for preservation purposes.

NEW BUILDING PROGRAM

Work continues on the new library building on the grounds of the National Institutes of Health; as of January 1961, construction was about two-thirds completed. The major factor affecting progress has been the extensive rock formations encountered and the subsequent blasting operations required. More recently inclement weather has caused some delays. Contracts have been awarded for shelving for the main stack areas and for most special library furniture and equipment. By agreement with the Public Buildings Service, the National Institutes of Health will provide complete maintenance services for the new building and grounds on a reimbursable basis. Plans are now being made to dedicate the new building in November 1961.

1962 BUDGET ESTIMATE

This estimate of $2,066,000 reflects an increase of $328,000 above 1961 requirements. The major part of this increase is for occupying and operating the new library building. In addition, the requested increase will permit continuation of interlibrary loan and reference assistance services at satisfactory levels and permit restoration of the program for converting to microfilm materials not serviceable because of poor physical condition. It will provide additional staff assistance to the Director, improved communication and copying services, and will permit increased coverage of the world's medical literature indexed in the Index Medicus.

Dr. ROGERS. I appreciate very much the opportunity to testify today. We have had a very successful year at the National Library of Medicine. We made progress on all fronts. Our services in all categories have increased.

It is fair to say that at no time during the last decade has there been a greater use of the facilities of the library than during this year just passed. We are expecting to move to our new building in Bethesda later on this year, and a large part of the increase that we are asking for is connected with this move. We have an increase of some $311,000 in the budget.

SUMMARY OF BUDGET

Mr. FOGARTY. Your appropriation for 1961 is $1,738,000 and the request for 1962 is $2,066,000, an increase of $328,000 and nine positions.

Dr. ROGERS. That is correct.

Mr. FOGARTY. I notice most of this increase is $265,000 for payment to the NIH management fund to which you are making no payments now. What is that for?

Dr. ROGERS. This is for maintenance charges on the building. At the present time in our old building there are maintenance charges for keeping this building, but these do not appear in our budget at all. These are part of the General Services Administration budget.

Mr. FOGARTY. I understand.

Dr. ROGERS. This makes it appear that this new charge is all brand-new when, of course, as a matter of fact, it is not.

Mr. Fogarty. General Services was doing the same thing for you in the old building?

Dr. Rogers. Yes, sir.

1962 PROGRAM INCREASES

Mr. Fogarty. Tell us why you need these nine additional positions and what they are going to do.

Dr. Rogers. Two of the positions we are requesting are for carrying on the work of the new Index Medicus. You will recall that last year was the first year of operation of this new index. Our report on the project has just come out. I would like to leave this with you if you care to see it.

Mr. Fogarty. Yes.

Dr. Rogers. One of the objectives in developing the new Index Medicus was to have an increased capacity for handling the larger volumes of literature which we did not have under our old system. We projected for 1960 that we would cover 125,000 articles, which is more than we ever did before, and we did make that goal. Our goal is to increase this to 136,000, then to 150,000, and ultimately 180,000.

We are asking for an increase of two positions, which are clerk-typist positions, in the Index Division to do the basic composition of this added amount of material which is going into the Index Medicus. These are two of the nine positions.

We are asking for three positions as microphotographers. Two years ago you allowed us an increase for supplies in the photography area on our plea to increase emphasis on our poor paper preservation program, that is, to get more of the library's materials which are deteriorating by reason of age onto microfilm before they disappeared.

The difficulty here has been that the poor paper preservation program and the interlibrary loan program—the program we have for sending out materials to people all over the country and all over the world when they ask for them—both utilize photography.

Our interlibrary loans constantly increase. During 1960 the size of the demand on us increased by 31 percent. They have increased this year so far another 18 percent. We must meet the interlibrary loan requests first out of the resources we have in the photography program. As these go up, the poor paper program has been terrifically depressed in amount. We want to restore this balance by adding three microphotographers to take care of the enormous increase in the demand which is made on us for materials.

Two positions are for better program management. We would like to establish the position of associate director of the library, get a younger Public Health Service commissioned officer into the library, get him trained, give me and my top staff some help in managing this whole program a little better. That is one of the two positions. Another is an extra secretarial assistant in the Office of the Director to handle the increased amount of work that is coming our way.

The other two positions are in the area of reference. We are going to be moving out to our new building in Bethesda, and we will find ourselves right in the middle of a tremendous medical community there, not only the National Institutes of Health but the Navy and even the Army being much closer to us there than they are now. We expect there are going to be increased demands on us.

We would like to open on Sunday, which we do not do now. We would like to provide for what we think will be inevitably increased demands for reference service. This accounts for the nine additional positions.

PROPOSED CHANGE IN APPROPRIATION LANGUAGE

Mr. FOGARTY. Doctor, we will put the portion of the justifications explaining this new language in the record, and then you supplement it with whatever you would like to tell us now.

(The material referred to follows:)

APPROPRIATION LANGUAGE CHANGE

Section 202, general provisions, of the General Government Matters Appropriation Act, 1961, provides that, with certain specific exceptions and unless otherwise specified, no part of any appropriation contained in any act may be used to pay the salary of a non-citizen employee whose post of duty is in the continental United States. A general exception is made in the case of nationals of countries allied with the United States in the current defense effort.

The Library's holdings exceed 1 million items, of which 80 percent are of foreign origin. Considerable effort is required to organize, maintain, and service this material. Yet positions established for the particular purposes of effectively utilizing our foreign collections cannot be kept filled because of our inability to obtain qualified personnel due to the present prohibition against employment of nationals from certain foreign countries.

From time to time the National Library of Medicine receives applications for employment from nationals of countries not allied with the United States in the current defense effort. In many instances these applicants possess outstanding qualifications for positions requiring proficiency in East European and Asiatic languages and substantial academic training and/or experience in the medical and allied sciences.

If it were permitted to employ noncitizens from countries not now allied with the United States, especially nationals from East European and Asiatic countries, the Library could more effectively discharge its responsibility for assisting the advancement of medicine and public health.

The requested language change would give the Library this authority. It is also noted that similar authority exists for the Library of Congress. This authority will be included in a legislative proposal to be submitted at a later date.

Dr. ROGERS. At the present time there is a prohibition in the statutes against hiring aliens. There is a general exception granted to this statute, which does permit the hiring of aliens who come from countries who are friendly to the United States in the defense effort. This is interpreted to mean, for example, that it is impossible for us to hire a Hungarian national, a person born in and a former citizen of Hungary. Hungary is not allied with us in the defense effort. The person in question may have been driven out of the country by force. Nevertheless, we cannot hire him.

Mr. FOGARTY. We ran into a lot of trouble last year on the matter of legislation in an appropriation bill. This is clearly subject to a point of order. If this is really important, you should start the wheels turning and get to the proper legislative committee and get legislation.

Mr. KELLY. We are doing that, Mr. Chairman, along with all the other items subject to a point of order that we think should be continued. We are endeavoring to draft basic legislation. Our request to you for this year is that, if at all possible, the Congress continue the point of order legislation in the 1962 Appropriation Act to give us a chance to get the necessary legislative consideration with a view toward there not being in 1963.

Dr. Rogers. There is a similar provision in the appropriation language for the Library of Congress.

Mr. Fogarty. Mr. Laird.

THE INDEX MEDICUS

Mr. Laird. I would like to take a look at this January 1961 publication of yours. Do you have it with you?

Dr. Rogers. The Index Medicus?

Mr. Laird. Yes.

Dr. Rogers. I do not have a copy of it, but I am familiar enough with it——

Mr. Laird. Is that a much bigger publication than this one [indicating]?

Dr. Rogers. We publish the Index Medicus each month, Mr. Laird, 12 months in the year. It varies a little in size from month to month.

Mr. Laird. Does this have the same information in it or is this just a supplement?

Dr. Rogers. Each month's material is entirely new. There is no repetition of previous months' work. The only unusual thing about the January issue each year is that we list there the names of all the journals which we index regularly. That appears only in the January issue each year for convenient reference.

Mr. Laird. This looks to me like a pretty valuable publication.

Dr. Rogers. It is the only publication of its kind. It is an absolute necessity to people all over the world. I have been very interested to see—I just saw the figures yesterday—the subscriptions to this publication in the last 6 months of 1960 increased by 1,325, which I think indicates a general acceptance of the new format and of the new program for this publication.

COST

Mr. Laird. I notice this publication sells for $20 a year.

Dr. Rogers. Yes, sir.

Mr. Laird. What is the cost of publication?

Dr. Rogers. The $20 is a price set by the Government Printing Office, and it goes directly to the Government Printing Office, of course, and not to us.

Mr. Laird. I understand that. I wondered if it offset the cost of producing such a publication.

Dr. Rogers. No. I believe it relates purely to the cost of printing the number of offprints needed to satisfy the subscriptions. The editorial cost is totally subsidized by the Government.

Mr. Laird. How much would this publication cost if we were not producing it on a subsidized basis? What is the editorial cost?

Dr. Rogers. $300,000.

Mr. Laird. How many subscriptions do you have?

Dr. Rogers. About 6,000. That would figure out at $50 per copy.

Mr. Laird. So that if the printing costs are $20——

Dr. Rogers. We have to add to that. The $300,000 does not include the GPO cost of printing these additional copies. It is only the editorial cost.

Mr. LAIRD. You would have to add $20 to the $50 and it would be $70 per year as the cost of this publication to the Federal Government?

Dr. ROGERS. Yes, sir.

Mr. KELLY. Which is a little less than $6 per copy per month.

Dr. ROGERS. The "Index Medicus" is an enormous thing. There were 125,000 articles listed in it last year, and each one of these was cited an average of 5 times each under 3½ subjects and 1½ authors. This means there are 625,000 citations in this book. It is an enormous quantity of material.

Mr. LAIRD. I think it is a very fine book. It is certainly a very necessary tool for a great many people interested in medical research and in medicine generally. But when I saw the price of it, I just could not believe you could do the work for $20 a year as this subscription rate is listed.

Dr. ROGERS. You cannot.

Mr. KELLY. I think this is true of all Government Printing Office publications. You are just paying the printing cost.

Dr. ROGERS. Yes, that is true of all Government publications.

Mr. LAIRD. You sell this for $25 a year, as far as foreign subscriptions are concerned; does that difference cover the extra postage?

Dr. ROGERS. GPO sets that price to take care of the extra postage. The $20 price applies in the United States and Canada, and the $25 price applies elsewhere. It is, of course, an expensive item to mail out. The bigger we make it, the more it weighs and the more the postage costs.

We mail out some copies of this which we exchange for substantial foreign publications, and there is a small item in here for increase in the postage, which will inevitably follow the increase in the size of the publication that we are expecting to get out.

Mr. LAIRD. That is all the questions I have.

Mr. FOGARTY. Thank you very much, Doctor.

TUESDAY, APRIL 11, 1961.

RETIRED PAY OF COMMISSIONED OFFICERS

WITNESSES

HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities: Retirement payments and survivors' benefits (total costs—obligations) (object class 13)	1,682	1,920	2,180
Financing: New obligational authority (appropriation)	1,682	1,920	2,180

GENERAL STATEMENT

Mr. FOGARTY. Mr. Doran, are you going to justify the retired pay of commissioned officers request?

Mr. DORAN. I have a short statement.

Mr. FOGARTY. We will put that in the record.

(The statement is as follows:)

Mr. Chairman and members of the committee, this appropriation provides funds for payments to retired commissioned officers of the Public Health Service and to survivors of deceased retired officers. These payments are mandatory and cannot be administratively controlled.

Under Public Law 86–415 approved April 8, 1960, all retired officers both Regular and Reserve are subject to the same laws and are paid from this appropriation. Prior to enactment of this legislation Reserve officers retired for reasons other than disability were subject to the Civil Service Retirement Act and paid by the Civil Service Commission. The new legislation also provides that, subject to certain limitations, any commissioned officer may retire upon the completion of 20 years of active service. By January 16, 1961, 12 officers had retired under the 20-year provision.

The estimate of $2,180,000 is based on a projection of the cost of beneficiaries now on the retired roll with allowance being made for anticipated additions and terminations.

As of January 16, 1961, 324 retired officers and 24 survivor annuitants were on the roll. It is estimated that there will be a net increase of 23 officers during fiscal year 1962.

Mr. FOGARTY. Is there anything unusual this year?

Mr. DORAN. Very little. There was a change in the legislation this past year which has increased the number of retirements somewhat. Other than that, the story is pretty much the same as for previous years.

Mr. FOGARTY. Is there anything else you would like to say?

Mr. DORAN. No, sir.

TUESDAY, APRIL 11, 1961.

OFFICE OF THE SURGEON GENERAL

WITNESSES

DR. JOHN D. PORTERFIELD, DEPUTY SURGEON GENERAL
HARRY L. DORAN, CHIEF FINANCE OFFICER
JAMES F. KELLY, DEPARTMENT BUDGET OFFICER

Object classification

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
11 Personnel compensation:			
Permanent positions	3,254	3,937	4,083
Positions other than permanent	18	19	19
Other personnel compensation	34	17	5
Total personnel compensation	3,306	3,974	4,107
12 Personnel benefits	274	343	353
21 Travel and transportation of persons	107	137	139
22 Transportation of things	10	12	12
23 Rent, communications, and utilities	194	209	208
24 Printing and reproduction	150	146	147
25 Other services	58	44	40
Services of other agencies	137	180	179
26 Supplies and materials	59	47	51
31 Equipment	49	41	39
Total obligations	4,342	5,132	5,275

Personnel summary

	1960 actual	1961 estimate	1962 estimate
Total number of permanent positions	559	599	609
Full-time equivalent of other positions	3	4	4
Average number of all employees	501	559	577
Number of employees at end of year	535	574	588
Average GS grade	7.5	7.7	7.7
Average GS salary	$6,255	$6,814	$6,841

Program and financing

[In thousands of dollars]

	1960 actual	1961 estimate	1962 estimate
Program by activities:			
1. Public health methods and reports	615	724	815
2. International health activities	135	142	170
3. Management and central services	3,614	4,266	4,290
Total program costs	4,364	5,132	5,275
4. Relation of costs to obligations: Costs financed from obligations of other years, net(—)	—22		
Total obligations	4,342	5,132	5,275
Financing:			
Comparative transfers to other accounts	1,338	2,236	
Unobligated balance lapsing	136		
New obligational authority	5,816	7,368	5,275
New obligational authority:			
Appropriation	5,816	6,900	5,275
Transferred from "Assistance to States, general" (42 U.S.C. 226)		142	
Appropriation (adjusted)	5,816	7,042	5,275
Proposed supplemental due to pay increases		326	

Mr. Fogarty. Who is going to justify salaries and expenses?

Dr. Porterfield. I am. I have a short opening statement which I can present.

General Statement

Mr. Chairman and members of the committee, because of the progress that has been made in the reorganization of the Public Health Service, the functions covered by the appropriation title, "Salaries and expenses, Office of the Surgeon General," for fiscal 1962, are somewhat different from those of the current fiscal year. Two substantial changes affecting the size of the 1962 estimate have been made in the composition of the Surgeon General's Office.

The first and most substantial of these changes is the transfer of the National Health Survey and funds in the amount of $2,553,000 to a newly created National Center for Health Statistics which will include, as you have heard, in addition to the functions of the National Health Survey, the National Office of Vital Statistics. The 1962 estimate for the National Center is continued in a new appropriation account which you just discussed.

The second major change in the Office of the Surgeon General is the addition of the Division of International Health to our family. For this Division we are making a budget proposal of $170,000.

A third change organizationally puts the Division of Health Mobilization in the Office of the Surgeon General. The budget for this

Division, however, does not appear in this appropriation since the work of this Division is financed from funds appropriated to the Office of Civil and Defense Mobilization.

The current fiscal year has been an active one, particularly in the matter of maintaining our course and direction in respect to present and future health needs of the American people. The increase of $100,000 granted by the Congress last year has made it possible for us to support studies of health manpower in several categories where the shortages are especially acute, and studies of the effect that various methods of financing medical care services have on the pattern of utilization of the services and on the cost of medical care.

The estimate of $5,275,000 for 1962 provides $57,580 for annualization costs and $112,800 for program increases. I would like briefly to sketch the distribution of program increases in terms of the functions which they would serve to finance.

In the Division of Public Health Methods we are asking for an increase of six positions and $63,600. We are proposing to use this money in furthering studies of the economics, the availability, and the organization of medical-care services in the Nation. Some of these studies have been started, others are now in the planning stage. They will provide the facts the Nation needs in mobilizing its medical care resources so as to make the most efficient use possible of scarce health manpower and facilities.

We already have reports and studies in process on health manpower in the medical, nursing, practical nursing, and public health social workers fields. We hare participating in studies which should give us detailed information on a number of other categories of health manpower such as medical technicians, dental technicians, pharmacists, and environmental health workers. We are planning further collection and analysis of material for the financing of medical care particularly as this relates to the various kinds of insurance or other third-party payments which are exercising an increasing and tremendous impact on the pattern of use in health services and manpower and directing the usage of service by the kind of coverage provided. For instance, insurance coverage which excludes outpatient services inevitably leads to the overuse of hospitals. It is with respect to the assessment and investigation not only of the components of medical care but also to the relationship between them that the Division of Public Health Methods has requested an increase.

For the Division of International Health, we are asking for an increase of two positions and $28,200. This reflects our growing participation in international matters, including staff support for the Surgeon General, relationships with the World Health Organization and its regional offices, and other international organizations concerned with health programs.

The Division of International Health also plays an active role in the growing exchange of health missions between the United States and the Soviet Union. To date there have been 10 Soviet missions to the United States and 9 United States missions to Russia, involving a total of 41 Russian and 44 American scientists. In addition, the United States and the Soviet Union are exchanging individual scientists and arranging technical meetings concerned with poliomyelitis, heart disease, and cancer under an official agreement between the two countries.

In the area of management and central services we are proposing to continue at substantially the 1961 level. The only increase proposed would provide two positions and $21,000 to assure careful and thorough program planning for our construction activities.

This summary statement gives you the highlights of our plan for the next fiscal year as more completely presented in the budget justification which has been furnished you. I shall be glad to answer any questions.

REQUEST TO BUREAU OF THE BUDGET, 1962

Mr. FOGARTY. What did you ask the Bureau of the Budget for?

Dr. PORTERFIELD. $6,309,000.

Mr. FOGARTY. Will you give us a breakdown of the reduction?

Dr. PORTERFIELD. Yes, sir.

(The information requested follows:)

REQUEST TO THE BUREAU OF THE BUDGET

The President's budget contains all amounts included in the request to the Bureau of the Budget except for $1,034,000 and 18 positions related to activities proposed by the Division of International Health. Approximately $1 million and 14 positions would have been used to develop a program of international medical exhibits designed to inform the world public of our progress in medicine. The balance would have been used to strengthen the staff engaged in drafting and reviewing policy position papers; participating in official international meetings; and discharging Public Health Service responsibilities in international health matters.

Mr. FOGARTY. Your increase this year is $143,000 and 10 positions?

Dr. PORTERFIELD. That is right, sir.

INCREASE TO COORDINATE CONSTRUCTION

Mr. FOGARTY. $21,000 of the increase requested is to establish an Office of Coordinator of Construction. Some of us have complained over the years that the main reason that your construction drags at times is that too many people have to get into the act. Now you want to put some more people into the act. How is that going to clean this up?

Dr. PORTERFIELD. We trust this will be a substitution, rather than an addition. The problems of daily management of our various construction accounts has been handled partly in the bureaus and in some degree in the Office of the Surgeon General and partly in the department which has entailed a considerable amount of coordination, as you say. We hope by the establishment of this position in the Office of the Surgeon General, with delegation to it of responsibility for detailed coverage, that we will be able to expedite these matters.

Mr. FOGARTY. Do you think this will help in your trouble with the GSA and the Budget Bureau in holding back some of these building programs?

Dr. PORTERFIELD. We expect this will increase and improve the efficiency of these contacts with the Bureau of the Budget.

AGREEMENT WITH RUSSIA

Mr. FOGARTY. What is the significance of the statement on page 259, "The Public Health Service is the only agency with a separate agreement with its counterpart in the U.S.S.R.?"

Dr. PORTERFIELD. In the agreements which have been established between this country and the U.S.S.R. in health, we do have a somewhat unique situation in that the agreement was written in terms of the Surgeon General making a direct approach and direct detailed agreements with the appropriate counterpart in the U.S.S.R. for the exchange of information and the exchange of missions in the health and medical research areas.

RADIATION HEALTH PROBLEMS FROM NUCLEAR-POWERED VEHICLES

Mr. FOGARTY. Doctor, I keep hearing about nuclear-powered missiles and planes. How will that affect us?

Dr. PORTERFIELD. A number of agencies are involved in developing aerospace vehicles which will be propelled by the application of nuclear energy. This includes projects on the development of nuclear reactors for ram jet propulsion and nuclear rocket propulsion. There are also devices planned for the development of auxiliary power for use on space vehicles. This program could introduce another source of radioactivity to the earth and its atmosphere. This source of radiation exposure to man would be added to that presently resulting from other uses of nuclear energy and the use of radiation producing devices and materials in the medical arts.

Mr. FOGARTY. Is this any different than the problems and areas you are already working in?

Dr. PORTERFIELD. The nuclear reactors associated with space planning can be categorized into ram jets, rockets, and auxiliary power sources. By far the largest of these are the rockets and ram jets. These latter devices will have power levels comparable to major nuclear electric power stations, but because of weight and other considerations they cannot have the built-in waste collection and treatment systems which are essential parts of stationary reactors used for electric power, or those for nuclear propelled vehicles like ocean vessels. There are also problems of contamination associated with reentry of some of the devices into the earth's atmosphere. The possibility of accidents involving very high speed vehicles loaded with fission products also exists. Even if the weapon component of these devices was not attached, or, if attached, did not explode, major contamination problems could, nevertheless, occur.

ACTIVITIES ASSIGNED VARIOUS AGENCIES

Mr. FOGARTY. In view of the safety activities of the Department of Defense and the Atomic Energy Commission, why is the Public Health Service involved in this?

Dr. PORTERFIELD. The Surgeon General, under section 301 of Public Law 410, has general responsibility for any or all health problems capable of affecting the Nation's health. The Public Health Service has also been assigned specific responsibility under Executive order for the measurement and evaluation of contamination from all sources of radioactivity. The PHS also can be expected to be looked to by the health agencies throughout the country, and throughout the world for opinions on the nature and probable effects of contamination from these devices. Presently, there is little information available on the actual discharge of radioactive material from these devices even under test conditions at fixed locations. It is essential that information be available on the nature and levels of discharge while these devices are in a fixed position as well as in flight, and that instrumentation be developed to measure the significant radioactive materials and radiations involved. It is important that we not only measure external radiation and some of the long lived particulates as we have in some of the weapons tests, but that we also measure some of the short lived radioactivity in gaseous and particulate form, and short term exposure to external radiation. Presently equipment for this purpose is either lacking, uncalibrated, or unassembled in working units.

Mr. Fogarty. How do you plan to do this work?

Dr. Porterfield. Our basic plan calls for assigning public health personnel who have had experience in other contamination problems, and to have them obtain available information from the AEC and the DOD and their contractors relating to the nature and amounts of radioactive discharge. On the basis of this information and such calculations as prove to be necessary, we will develop tentative models of potential exposure. On the basis of the models, test instrumentation will be designed and procured. This instrumentation will then be evaluated during the course of field trials of the nuclear power units undergoing testing in the field. From this we will develop systems of known reliability which can be used to estimate the exposure of people to either the test devices of the United States and its allies or those of unfriendly powers, or in the case of war, to assess the exposure from these devices together with other implements that may be used.

BUDGET FOR PHS ACTIVITIES IN FIELD

Mr. Fogarty. Yes, but what are you doing in the immediate future? What do you propose to do under this program that you have presented in this budget? I do not recall your mentioning any money to be used for a program on this problem.

Dr. Porterfield. Yes, sir; that is correct. As you know, this budget and program was made up more than 6 months ago and no program was planned specifically for this aerospace area. However, in light of the site visits and discussions with other agencies which have recently occurred, we realize that the need to deal with these problems is immediate and urgent. We are currently developing a plan for the initial phase of this work.

Mr. Fogarty. Are you going to get out of this initial planning that you refer to and take some action on this problem during the coming fiscal year?

Dr. Porterfield. As I indicated a moment ago, our current budget proposal does not provide funds for this program, so any active program work would have to be limited, at best.

Mr. Fogarty. If we are going to have these vehicles flying around over the country, it seems to me you should be moving faster than that. What would it take to really get a program going on this next year?

Dr. Porterfield. Our basic plan for the first phase calls for a scientific staff of approximately 30 positions, primarily located at our Las Vegas laboratory. In addition, equipment, supplies, and animals must be obtained to carry out the basic assessment work and to develop methodology for the more advanced work that must be undertaken. We estimate the first-year cost of such a program at about $600,000.

Mr. **Fogarty.** Mr. Marshall?

COMPARATIVE TRANSFER IN 1961

Mr. **Marshall.** In your statement you state that you transferred to the newly created National Center for Health Statistics $2,553,000. I note on page 218 of the justification that they state that they received a transfer of $2,236,200. What happened to the difference between the two?

Dr. **Porterfield.** The $2,553,000 represents the amount to be transferred from the Office of the Surgeon General for 1962. The $2,236,200 is the 1961 amount.

Mr. **Fogarty.** Mr. Michel?

Mr. **Michel.** No questions, Mr. Chairman.

Demonstration Grants Under Public Law 660

Mr. **Fogarty.** Dr. Porterfield, I spoke to the Surgeon General about getting us a statement on the need for demonstration grants under Public Law 660. Is that statement ready?

Dr. **Porterfield.** Yes, it is.

Mr. **Fogarty.** Please place it in the record at this point.

(The statement referred to follows:)

Department of Health, Education, and Welfare—Public Health Service, Division of Water Supply and Pollution Control

DEMONSTRATION GRANTS UNDER PUBLIC LAW 660

Since passage of the Federal Water Pollution Control Act in 1956, there has been a growing interest in demonstration grants. This authorization of the act never has been implemented because of a lack of funds. Such grants could be made to public and private agencies, individuals, and institutions.

A demonstration is a useful means of disseminating the findings of research. These grants would be timely now, because of a buildup in water pollution research which will provide more principles for demonstration. By demonstrating a workable plan to handle water pollution, those confronted with similar problems can apply their new knowledge to their own problems.

Research grants seek to develop new knowledge whereas demonstration grants are designed to test the reliability and application of knowledge already developed. Demonstrations also serve to spread this knowledge widely and to train persons to apply this knowledge.

A most valuable product of demonstrations is the shortening of the time periods from development through research and from studies of new or improved treatments or pollution control methods to their incorporation into routine engineering practices. Without demonstrations, the "gestation" period is at best 10 years, but more often from 15 to 20 years. Large sums of money are spent in construction and operating costs during these long periods. Money could have been saved had the advantages of new developments been proven and made known. Demonstrations can greatly speed up application of new principles and procedures by proving their utility and reliability. Thus proven, design engineers and others can confidently put them into practice without waiting for time alone to test their application.

Numerous inquiries as to the availability of funds to support demonstration projects on a wide range of appropriate subjects have been made by individuals, agencies, and institutions from virtually every section of the country. Five examples of specific demonstration project proposals are attached. These would require approximately $1 million for their full support over the period of their operation.

Agencies, institutions, industries, and individuals obtain much valuable water pollution information which is not widely known or which requires demonstration of applicability to pollution situations. Demonstration grants would stimulate and encourage the sharing of such information with others, thereby greatly increasing the available knowledge to deal with water pollution.

To date, inquiries made and proposals received indicate that the availability of demonstration grant funds would result in many proposals for much-needed projects and would attract highly qualified demonstrators in many fields. The need for demonstrations increases as water pollution problems continue to multiply in number and complexity.

TYPICAL EXAMPLES OF REQUESTS RECEIVED FOR DEMONSTRATION GRANTS

1. Tennessee Fish and Game Commission—for a series of five projects to demonstrate the effects of various pollutants on the fishery resource, the first of which would be a demonstration of the effects of wastes from a new paper mill on one of the most important fishing areas in the State.
2. Sanitation Council for Southeast Michigan—a cooperative project to demonstrate the development of a rational plan for sewerage and drainage in a metropolitan area, including intermunicipal financing, operation and maintenance (demonstration area to be the six counties of the southeastern Michigan metropolitan area).
3. The Ohio State University—to establish an experimental area to demonstrate procedures for monitoring mine acid wastes and the applicability of mine seals for controlling such wastes.
4. New York City, for a project to demonstrate a procedure and the value of mapping and inventorying all waste discharges into the streams and harbors of the metropolitan New York area.
5. University of Southern California—an oceanography project to demonstrate rational approaches to determine—
   (*a*) the fate of organic substances and nutrient elements in sewage discharges into the marine environment, and their effects on biological productivity;
   (*b*) the survival of enteric pathogens in the sea; and
   (*c*) biological indicators of radioactive contamination.

   (This project is proposed to cover a period of five years.)
6. Offshore fresh water resources—geological investigations have demonstrated that there are significant fresh water resources offshore of heavily populated areas. A project for tapping these resources below the ocean floor and demonstrating their value for augmenting agricultural, municipal, and industrial supplies has been proposed.

Menominee Indian Health Clinic

Mr. Laird. Mr. Chairman, I would like to have a statement placed in the record to show how much it would cost to operate the health clinic for the Menominee Indians during 1962.

Dr. Porterfield, could you ask Dr. Shaw to prepare an estimate on that for the record?

Dr. Porterfield. I would be glad to.

(The requested information follows:)

Cost of Operating a Health Clinic for the Menominee Indians for Fiscal Year 1962

Based upon the assumption the Division of Indian Health could renegotiate the existing contract, it is estimated that the cost of operating a health clinic for the Menominee Indians for fiscal year 1962 would amount to $32,000.

This estimate is broken down as follows:

Physician	$10,000
Registered nurse	4,200
Welfare screening and clinical	6,000
Drugs	6,000
Medical supplies	3,000
Subtotal	29,200
Facilities, tribal	3,000
Total	32,200
Rounded	32,000

Based upon 3 months' experience, it is estimated the average units of service for fiscal year 1962, on a monthly basis, would be as follows:

Preventive services	313
General medical care	792
Prescriptions	694
X-rays	26
Laboratory tests	22

Mr. Fogarty. Is there anything else you would like to say, Doctor, before you conclude for the Public Health Service?

Dr. Porterfield. No, sir. Dr. Terry is sorry he could not be here this morning. We appreciate very much the courtesy shown and we would be glad to provide any further information now or later.

Mr. Fogarty. Thank you very much.

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